W. S. Adams

BLOOD TRANSFUSION
HEMORRHAGE AND THE ANÆMIAS

BY

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TO
H. M B.

PREFACE

The present volume is an outgrowth of a chapter on Blood Transfusion written in 1913 as part of a monograph published in that year on Surgery of the Vascular System. After a very gratifying distribution of that work, a revision seemed in order because of the many advances made in this field of surgery, but on addressing myself to the task, I was amazed at the development attained by the subject of transfusion to which just one chapter had been devoted only a short time before. Such revolutionary changes in technic had come about and the usefulness of transfusion had developed so tremendously that it seemed wise to postpone the contemplated revision, and to prepare a separate work with the single topic of blood transfusion. An enormous amount of work has been carried out in recent years by hundreds of enthusiastic investigators as a result of which a vast literature has arisen, still there has been no compilation of the subject since Crile's work on "Hemorrhage and Transfusion" in 1909, before transfusion had proved itself of practical, enduring worth.

Crile's stimulating book was devoted mainly to the experimental aspect of transfusion, although its clini-

cal side was considered as far as was possible at that time. The book has never been revised for reasons best known to its author, but the probabilities are that, having pointed the way, Dr. Crile's interests led him into other fields. Under these circumstances, it seemed that a compilation setting forth all the various methods of the present day, with a consideration of the indications for transfusion, and a brief appendix containing pre-transfusion tests might be timely.

It has been my purpose to adhere to the practical side of the subject, both as regards discussions of indications, and selection of transfusion methods. Theoretical considerations have been eliminated as far as possible, and the future uses to which blood transfusion may be put have hardly been suggested, since the book is meant for the man who is engaged in clinical work of this nature, and desires to know concretely what is being done and how to do it. Those interested in the laboratory side of blood work are referred to the abundant literature, references to which have been selected with utmost care, in regard to both the clinical problems and the abstract phases of the subject.

Bertram M. Bernheim.

2313 Eutaw Place,
Baltimore, Maryland.
May, 1917.

FOREWORD

It is due to the author of this work to state that his sudden departure for foreign war service as a member of the Johns Hopkins Base Hospital Unit, has caused his treatise to be issued without opportunity for his final inspection and revision. Under these conditions indulgence is requested for some omissions and inadvertences which would have been corrected under normal circumstances.

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HISTORICAL NOTE

INVESTIGATION of early records indicates quite clearly that the inherent possibility for benefit from blood transfusion was recognized hundreds of years ago, and *bona fide* attempts to carry out the procedure are noted as early as 1492, when a transfusion failed to save the life of Pope Innocent VIII. Three youths are said to have lost their lives as a result of the trial. Following this, sporadic transfusions are found, notably one in 1667, by Jean Baptiste Denys, physician to Louis XIV. And it was about this time that Richard Lower, a physiologist, devised a practical method of direct transfusion almost identical with one the author thought he had originated about two hundred and fifty years afterwards! Lower conceived the idea of running blood from the vessels of one individual into those of another by means of two or more segments of goose quills interposed between the severed ends of the vessels, while the author accomplished the same purpose by means of a two-pieced silver tube as portrayed on page 97.

The trials of the early years are interesting as indicators of the modern trend of thought, but furnish little of value concerning actual blood transfusion

because the idea was too far in advance of anatomical and surgical knowledge and practice of the times. Harvey's discovery of the circulation of the blood did not appear in print till 1628, so there is little wonder that progress in a matter so intimately dependent on knowledge of the circulation was delayed and uncertain. Not until 1892 was any real progress made. At this time Von Ziemssen reported on a method of indirect blood transfer by means of needle and syringes, which was of some practical utility though it was far from satisfactory. His method made little impression, fell into disuse, and little was heard of it till some twenty or more years later when it was revived and perfected by Dr. Edward Lindeman, with whose name the method is now associated.

In reality the history of blood transfusion can be divided into four rather sharply defined divisions which are as follows:

First: That of the early abortive, sporadic attempts, the period dating from the year 1492 with the historic transfusion carried out in the effort to save the life of Pope Innocent VIII, to Carrel's work on the blood vessels, which marked a turning point.

Second: The truly epoch-making experiments of Carrel in which he devised the present day technic of handling blood vessels, and paved the way for Crile's work on blood transfusion. To Dr. George W. Crile,

of Cleveland, must go the credit for having devised and perfected the first practical method of carrying out this operation, and for having by this method awakened renewed interest in a procedure, long discarded because of the impossibility of securing an accurate blood transfer.

This second period may be designated the period of Direct Transfusion, for Crile's work incited many who enthusiastically set to work and in short order devised various ingenious instruments, all calculated to facilitate and simplify the direct flow of blood from one individual to another. Crile's little tube was early overshadowed because, though quite practical and constant in its results, it demanded a degree of skill for its proper handling that was found unnecessary for the successful use of subsequently contrived instruments. The names of Carrel, Payr, Crile, Elsberg, Brewer, Ottenberg, Levin, Lespinasse, Soresi and many others are linked with this period to whose development the author hopes he is not presumptuous in venturing to believe that he contributed a share.

The Third Period is that of Indirect Transfusion of whole blood, and dates from Lindeman's revival in 1913 of Von Ziemssen's old method. Other methods such as that of Curtis and David had been suggested for indirect transfusion prior to Lindeman's report, but it must be granted that this method found little favor

until the needle and syringe system came into vogue—and then it gradually became the method of election. The reason for its popularity was that, in addition to requiring very small incisions or (in certain instances) none at all, the amount of blood could be accurately measured—an impossibility by any of the methods of direct transfusion extant. Modifications of Lindeman's suggestion have been many and diverse and several are far simpler than his in their execution. The chief workers of this period are Lindeman, Unger, Miller, Kimpton and Brown, Satterlee and Hooker, Vincent, Percy and a host of others among whom the author again craves permission to include himself. The instruments these men perfected are responsible in great measure for the rapid development of transfusion and its growing popularity as a reliable therapeutic measure.

Beside the increased knowledge concerning the technic of blood transfusion, the third period is also notable for the general recognition it inaugurated of the necessity for carrying out tests for hæmolysis and agglutination prior to transfusion, and for the development of the requisite tests. With this work Moss' name is closely linked since he first showed that practically all people may be divided into four groups as regards their blood and that only those should serve as donors whose blood is in the same

group as that of the recipient. Ottenberg and Kaliski, Epstein and Ottenberg, Vincent, Whipple, Hess, Brem, Minot and others also did work along these and related lines, some of which was carried out before the beginning of the Third Period. But the real fundamental importance of the subject was unfortunately delayed until the increasing facility for carrying out transfusions gave rise to an increasing number of accidents that were shown to be due to a failure properly to group those participating in the operation.

The Fourth Period is just beginning and may well be termed the Period of Anticoagulation or Indirect Transfusion with the Aid of Anticoagulants. The desirability of having blood in an uncoagulable state has long been uppermost in the minds of those most intimately acquainted with transfusion problems, and the sporadic attempts to use defibrinated blood may be taken as manifestations of this feeling. But defibrinated blood proved a dismal failure and anticoaggulants of a chemical nature were always considered unsuitable for practical purposes because of their well-known toxic properties. Thus matters rested until in 1913–14 the work of Dr. John Abel, the well-known Pharmacologist, on Plasmaphæresis caused renewed interest in this phase of the subject by demonstrating the efficacy of hirudin in preventing blood coagulation in the dog without harmful effects. Following this, in

1914, Satterlee and Hooker reported on an ingenious and safe method of using hirudin for human transfusions, but the method never became popular because of the rather cumbersome technic and because of the known toxicity of hirudin. And in addition commercial preparations of the substance have always been rather unreliable.

Thus, little real progress toward the widespread use of anticoagulants was made, until the work of Hustin, Weil, Lewisohn and Agote, in 1915, rather unexpectedly placed the method on a firm footing. All four of these men, working independently of each other, came to the conclusion that sodium citrate, long known to pharmacologists for its anticoagulant properties, could be used in the human with perfect safety provided care was exercised in securing the proper dilution. Elaborate experiments on animals proved the correctness of their contention and now the sodium citrate method of indirect transfusion of blood bids fair to supplant all previously known methods.

Thus, the procedure of blood transfusion has evolved in successive stages from an undertaking of the most difficult and dangerous character, resorted to upon the rarest occasions, to a procedure of such simple and harmless character that it is utilized throughout the civilized world many, many times each day. Hundreds of people have been saved from

premature death from hæmorrhage, and the number of conditions in which it is utilized for therapeutic benefit is constantly increasing. Still, we are only on the threshhold of knowledge concerning the fundamental character of the procedure, and the uses to which it will eventually be put. Even now studies are in progress, and cases have been done with gratifying results, where only the cellular content of the blood has been used, an outgrowth of blood transfusion that could have come about only through the use of anticoagulants, and one that may prove to be of far-reaching import.

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CHAPTER I

BLOOD AND THE PHENOMENON OF BLEEDING

Loss of blood is such a common-place every-day affair in the lives of most people that its analytical consideration except under unusual or alarming conditions might seem almost foolish were it not for the fact that many features connected with it are most obscure, and its very commonness has a tendency to breed a degree of indifference that sometimes results in disaster. Confined in a set of hollow elastic tubes whose calibre varies tremendously, whose walls are so coarse in certain localities as to be able to withstand enormous pressure and so delicate at other places as to be invisible to the naked eye, whose ramifications penetrate to the uttermost limits of the whole body, blood is a constantly circulating liquid of such limited volume that comparatively small losses give rise to profound disturbances. It is possessed of a most remarkable property, that of coagulation, without which there could be no preservation of life, yet it remains con-

stantly fluid while within its channels, certain diseased states excepted—and day and night, year in and year out, instigated by the ceaselessly beating heart, it carries sustenance throughout its domains.

So long as all is well, scarcely any attention is paid to it. Only derangements are worthy of notice, and fortune has endowed the blood with one other quality of such nature that many and repeated insults are borne with equanimity, and derangements often pass unnoticed until they have become serious—so serious as to be at times irreparable; for in addition to its quality of fluidity within its channels and that of coagulation outside of them, blood has a still further power—that of regeneration, through which means losses are, under certain circumstances, retrieved. Equipped in this threefold manner, the blood is able to care for itself so satisfactorily that trifling derangements pass unnoticed, and even those of greater magnitude frequently give little concern, a rather unfortunate circumstance from certain view-points because it gives rise at times to a false security that a more sensitive registering mechanism would not tolerate. If the blood could notify us of its minor disturbances, we would necessarily form the habit of more frequently examining it, and consequently would be able to recognize in an early stage conditions which, under present circumstances, are only apparent when far advanced.

Particularly is this true of the anæmias, affections so slow in their onset and so insidious that such hints as increasing pallor, shortness of breath, weakness, are danger signals usually sounded too late. If there were some more urgent sign, we might be of greater service.

Before discussing the various kinds of hemorrhage, it may be well to point out that blood may be lost in different ways, some of which are not serious, while all are capable of becoming so, and that the same type of bleeding in many cases may arise from any one of a number of causes. So a simple tabulation of the different kinds of hemorrhage can do but little more than concretely picture various possibilities, the actual diagnosis of a given condition depending mainly upon the discriminating powers and experience of the physician in charge.

It seems wise to divide hemorrhages into two classes, *concealed* and *unconcealed,* which means that all bleeding is either apparent to the eye, or non-apparent. The intra-abdominal hemorrhage from a ruptured liver is an example of the first, while the bleeding from lacerated tissues is a type of the latter. It is obvious that both concealed and unconcealed blood loss may be the result of some accident.

Pulmonary hemorrhages are always unconcealed, as are in reality bleedings from the intestinal tract,

but because it sometimes requires hours or days for the blood to pass out, this latter form is usually cited under both the concealed and unconcealed bleedings. Uterine bleedings must be tabulated as of this sort, too, because of the inability of the blood to get out under certain conditions, and because of the intra-abdominal hemorrhage accompanying ruptured extra-uterine pregnancy. In fact, nearly all bleedings fall under both headings, and for similar reasons. For example, a post-operative hemorrhage is apparent, depending upon whether or not the wound has been closed or drained, or whether the drains have been packed in so tight as to amount to a closure. Hemorrhage from the urinary system is apparent, if it is passed, but it is not always passed and therefore remains concealed perhaps until a catheter is placed into the bladder. The slow bleedings resulting from defective coagulation are of both varieties, while intracranial hemorrhages, unless due to great violence, are always concealed. The simple table outlined below will serve as an approximate guide.

With one exception, that of menstruation, bleeding is a pathological process and should always be regarded as such, since the blood can only serve its purpose when within its own confines. It is possible that the blood loss known as menstruation is pathological, but since it occurs regularly each month dur-

ing certain years in the lives of practically all women, the conclusion can hardly be escaped that it is a normal affair. Why it begins at a definite period of life

Hemorrhage

CONCEALED

- I. Traumatic
- II. Non-traumatic
  1. From the alimentary tract
     - Nasal
     - Œsophageal
     - Gastric
     - Intestinal
     - Rectal
  2. In any of the body cavities or tissues
     - Cranium—ruptured blood vessel—apoplexy
     - Chest — ruptured aneurism
     - Abdomen
       - Ectopic
       - Aneurism
       - Ruptured organ
       - Ulcer
       - Intra-intestinal
       - Bladder
  3. Uterine
     - Separated placenta
     - Ectopic pregnancy
     - Menstruation retained
  4. Consequent upon defective coagulation apparatus (hemorrhagic group)
  5. Post-operative

UNCONCEALED

- I. Traumatic
- II. Non-traumatic
  1. From the alimentary tract
     - Nasal
     - Œsophageal
     - Gastric
     - Intestinal
     - Rectal
  2. Pulmonary
  3. Uterine
     - Menstruation
     - Ulcerated growth
     - Pregnancy
     - Post partum
     - Placenta prævia
     - Idiopathic
  4. Consequent upon defective coagulation apparatus (hemorrhagic group)
  5. Post-operative

and ceases at an equally marked period may have its apparent explanation in the beginning and cessation of ovulation, but this fails to explain why a true hemor-

rhagic condition should necessarily accompany ovulation at all. It must not only be regarded as normal, at present, but it must be granted that it causes little or no disturbance, such as might be expected in a similar periodic loss of equal amounts of blood under other circumstances. Its discussion in detail would be out of place in a work of this kind, except in so far as menstruation becomes abnormal and causes disturbances of such character as to require interference. These will be considered in their proper place.

Accidental bleeding is of common occurrence, especially minor varieties, and usually gives rise to little or no anxiety. The coagulatory apparatus of the blood comes to the rescue unbidden and usually stops the leakage very promptly. As a consequence, a carelessness concerning these matters has arisen that at times causes serious results, because it occasionally happens that the coagulative powers of the blood are unable to check the flow unaided. Further experience has shown that in such cases the longer the bleeding continues the more difficult the task of stopping it becomes. The reason for this is not clear, though the attempted explanation is that a derangement of the coagulatory apparatus takes place and becomes progressively worse, though just what this derangement is or why it should occur in certain instances and not in others, remains obscure. It is also baffling to know

that this phenomenon may occur in individuals who are in no sense bleeders, hæmophiliacs, although it is possible that future studies may place them in that or some allied category. It is rarely the great vessels that cause trouble of this sort, for if they are injured in any way strenuous efforts are made immediately to stop the flow. The hemorrhage of *violence* is usually of such nature that it peremptorily demands immediate attention and secures it.

But the vast majority of bleedings make no such demands and as a consequence frequently go unheeded. Who ever thinks of bothering about a little blood after tooth extraction? yet there are authentic cases of people losing their lives from such an insignificant thing. Quite recently it was necessary for me to work for three hours to control bleeding of this nature that had been neglected by the dentist for over twenty-four hours, the patient being an elderly woman who had borne eight children and had never before had trouble of a similar kind. And nose-bleeds—how they are neglected! By many they are considered evidences of good health! Even bleeding following nasal operations too often goes unheeded. About two years ago I saw a young physician who, ten days following an operation on his sinuses, had had a hemorrhage of such severity that it was controlled only by packing. In forty-eight hours the packs were removed and the

patient sent home. A day or two later the bleeding recurred, and the nose was again packed. With the knowledge of the previous hemorrhage still fresh in mind, the surgeon in charge might have exercised more judgment about removing his packs; but he was so fearful of meningitis from the damming up of secretions consequent upon prolonged tamponing, that he felt it unwise to leave them in. He had handled successfully so many similar cases of bleeding in this manner that it never occurred to him that he might be dealing with something just a bit different from the common variety. Nor could he be convinced that this case was the rule-proving exception until his patient had become so frightfully exsanguinated by repeated hemorrhages that his life was only saved by an emergency transfusion, and by nasal packing that was left *in situ* for ten days before being finally removed.

To have uterine bleedings of an obscure, stubborn, neglected variety is a common occurrence. There is hardly a woman who at some time during her life has not suffered with bleeding of an abnormal kind, different from her usual menstrual flow. In many cases, it starts spontaneously and ceases spontaneously, probably being due to some slight abnormality which rectifies itself; while occasionally such blood loss starts from an unrecognized cause but fails to cease without treatment. Cases are even on record where complete

removal of an apparently normal uterus was necessitated by continuous unchecked bleeding. Sloughing fibroids are of course a common cause and the menopause is a favorable time for vicarious bleeding to start up, although when there are no demonstrable uterine abnormalities it is hard to understand the bleeding. In October, 1913, I was asked to see a case of this type, in which the bleeding had progressed so far that the patient was too weak to speak above a whisper. She had failed to call in her medical adviser until the flow had been going on for weeks, but when he did finally come there was little to account for the trouble, and the usual forms of treatment failed to give relief. A transfusion of blood from one of her sons caused an immediate cessation of the bleeding, and a prolonged but uneventful convalescence ensued. It was thought that the menopause would take its normal course—she was at the appropriate age—but for three years thereafter this woman menstruated normally and was in perfect health. At the end of that time, a similar intractable bleeding set in for the relief of which a panhysterectomy was performed by Dr. W. W. Russell. The specimen revealed a carcinoma of the body of the uterus.

Gastric and intestinal bleedings are practically always the result of some ulcerative process that involves vessels of larger or smaller calibre, as the case

may be. They may be difficult to locate and treat but are not as a rule difficult to understand, except that group of cases coming under the head of hemorrhagic diseases. Some of these latter may be due to infection, possibly all are, but, if so, the infectious agency has not been demonstrated. They seem to come in certain cases from developmental errors of coagulation, but whatever their source the condition is always most dangerous. Further consideration will be given this subject later on.

More obscure than the ordinary intestinal bleedings are those cases of bleeding into the tissues to which the group name of purpura is given, and in which the blood appears literally to seep through the blood-vessel walls. Sahli holds that this phenomenon is made possible by an inherent developmental defect in the makeup of the vessel wall, but according to Duke it is due to an almost total lack of platelets in the blood. In mild cases only the subcutaneous hemorrhages are seen but the deeper tissues may be affected, and in certain severe cases bleeding into the internal organs probably occurs. In fact it is in this way that some of the unaccountable renal hemorrhages are explained. In the later stages of purpura—and in the later stages of all the hemorrhagic group of diseases—all the mucous membranes become affected and "weep" a thin uncoagulable blood. In November,

1914, I transfused such a case, the patient being a stalwart young farmer, but the best I could do was to secure a remission of a few months. Following the transfusion, the bleeding ceased and a marked improvement set in, but the inevitable relapse came along a few months later and the patient died.

This leads us to a consideration of that remarkable condition known as hæmophilia, recent research in which seems to affirm that there is a definite abnormality in the blood coagulatory apparatus of those afflicted with the condition. A theoretical discussion of the matter would be out of place in a work of this practical character, but a clear understanding may perhaps be gained by a brief study of the mechanism of normal blood coagulation according to the principles of Dr. W. H. Howell, of the Johns Hopkins University, who has probably done more work in this field than any other investigator.

Howell believes that antithrombin, present in small amounts in normal blood plasma, binds the normally present prothrombin and renders it inactive, that is, unable to start clotting of the blood. But whenever there is any cell injury (tissue, platelets, blood-cells, etc.) a substance called thromboplastin is set free which immediately neutralizes the antithrombin. This frees the prothrombin, which is thus enabled to combine with calcium to form thrombin. The free throm-

bin coagulates the fibrinogen, giving rise to the normal clot. His theory then is as follows:

$$
\begin{tikzcd}[column sep=small]
 & \text{Antithrombin} & & & \text{(thromboplastin)} \arrow[lll] \\
\text{Prothrombin} \arrow[drr] \arrow[ur, leftrightarrow] & & & & \\
 & & \text{(Thrombin)} \arrow[dr] & & \\
 & \text{Calcium} \arrow[ur] & & \text{(Clot)} & \\
 & & \text{Fibrinogen.} \arrow[ur] & &
\end{tikzcd}
$$

With this as the basis of his studies, Howell first proved that, as compared to normal blood, there is a most marked delay in the spontaneous coagulation of the hæmophilic blood—and that "the deficient coagulability was due to some permanent alteration in the properties of the blood." These deficiencies resolved themselves finally into an actual subnormal amount of prothrombin in the circulating blood and, since antithrombin was proved to be present in normal or slightly supranormal amounts, Howell concluded that "the essential condition in hæmophilic blood which is immediately responsible for its delayed coagulation is a subnormal amount of prothrombin in the circulating blood." He therefore says, "Hæmophilia may be defined as a condition, limited to the male, in which

the coagulation time of the blood is markedly prolonged in consequence of a deficiency in the amount of the contained prothrombin, with the additional characteristic that the defect is transmissible by heredity in accordance with the so-called law of Nasse."

This is not only a scientific but a satisfactory clinical definition of the condition as well, though it should be understood, in addition, that there may be spontaneous cases as well as hereditary ones. Howell himself reports one such instance of the disease, and there are others on record in which careful investigation fails to reveal the faintest hereditary cause; there are also many recorded cases of the so-called "bleeding tendency," that is, of individuals who bleed much more freely than they should, and longer, and on slight provocation. Perhaps if the blood of these people were subjected to careful investigation, it could be demonstrated that they are either true hæmophiliacs or of a class closely allied. Certain it is that there are many individuals who, while not actual bleeders, are always worried over bleedings that ordinarily cause no anxiety whatever, and they are justly anxious, since it is always rather trying to stop their bleeding, and as a result they must forego the comfort and convenience of many minor operations. Whether these unfortunates ever actually become true hæmophiliacs or not, I do not know, but I have had to transfuse a patient (the doc-

tor mentioned above) who was known to possess this bleeding tendency from the experience of two operations previous to the one in which hurried transfusion was all that could arrest an exsanguinating hemorrhage. Oddly enough, he has subsequently withstood an operation for acute appendicitis without difficulty.

Still other forms of spontaneous bleeding are occasionally encountered, in which icterus is a more or less predominant feature. Certain forms, according to the work of Whipple, seem to fall in the group of the so-called true hemorrhagic diseases, but the majority are caused by conditions resulting from obstructive types of jaundice. All are most dangerous, and it is sad to relate that the therapy is unsatisfactory.

Finally, there remain for consideration those cases of anæmia associated with actual blood disease, such as pernicious anæmia, the leukæmias and the anæmia accompanying malignant disease. These invisible bleedings, for they are so, usually go unnoticed until the host is weakened to such extent that an investigation as to cause is instituted. Actual bleeding may never take place, but it is common to note little hemorrhages from the mucous membranes late in the course of most cases, and they are always of bad prognostic significance. Occasionally, prompt measures may stop them for a while, but the conditions in which they occur are progressive, and recurrence is the rule. Toward

the end, it is not uncommon to find every mucous membrane "weeping" the thin uncoagulable blood that portends dissolution. A more detailed consideration will be given this topic later on.

The above introductory survey makes it evident that blood may be lost in many different ways and from a host of causes, some of which are understood, while others are still obscure; that even the most insignificant bleeding may resolve itself into a hemorrhage of most alarming character, and that, with this knowledge, there is little excuse for the prevalent indifference to blood loss of the minor grades. The successful study of hemorrhage, and hemorrhagic conditions, depends upon a broad conception of the many factors involved in causation and control, to which an understanding both of general medicine and surgery is indispensable.

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CHAPTER II

DIAGNOSIS OF HEMORRHAGE

DIFFERENTIAL DIAGNOSIS BETWEEN CONCEALED HEMORRHAGE, SHOCK, GENERAL PERITONITIS, HEART COLLAPSE, PERFORATED GASTRIC ULCER AND ACUTE PANCREATITIS

Loss of blood in any considerable quantity is accompanied by a sequence of signs and symptoms which are of such character as to be unmistakable in the majority of instances, but which are, unfortunately, not classically characteristic of hemorrhage alone. So that, where there is no visible evidence of bleeding and conditions are such that, although hemorrhage is strongly suspected, any one of a number of other causes may be responsible for the trouble, a proper diagnosis can only be reached by a judicial consideration of all those maladies which might give rise to the signs and symptoms encountered.

To take up the matter basically, of first importance is an accurate past history, a thing sometimes very difficult to secure. The patient may be reticent because of a desire to conceal an indiscretion—as in the case of an unmarried woman suspected of having a ruptured ectopic pregnancy—sometimes the doctor is

careless in his questioning, but more often the anxiety of the patient and relatives is so intense that important details of the past history are actually forgotten. In general, though, a true detailed statement can be had with care and patience, and one has only to look back over one's obscure cases to realize how clear some of them might have been had a little more care been exercised in obtaining an accurate history.

Next in importance to the previous history is the method of onset and, in sequence, the course of progression of the illness until finally the time comes for an intensive study of all features of the case in hand, including actual physical examination of the patient and laboratory tests of every available kind. Where haste is necessary (and time is an important element) certain steps in the examination must be eliminated, but to slur over laboratory tests because they are thought to have no bearing on the case is as reprehensible as is failure to inquire into the past history. Frequently it is the unexpected that happens and light is shed from a surprising quarter.

A cold clammy skin, a pulse of little force and less volume, but extreme rapidity and a little irregularity, a breathing hardly perceptible but rapid, a pinched expression, facies cadaverously cyanotic, a blood-pressure steadily falling and a patient in profound prostration—hemorrhage? Possibly. These are the usual

signs certainly, but they are usual for conditions other than hemorrhage as well. And if there is air-hunger, with sighing attempts to get air, instead of the shallow rapid breathing, and an increasing restlessness—hemorrhage? Almost certainly, but not necessarily. Broken compensation in an old cardiac case quite commonly is accompanied by air-hunger and restlessness, but a careful history might rule out this condition even if an examination should fail to do so—yet once in a great while neither of them will. But what about the blood findings? In general they are of little immediate aid, because the compensatory tightening up of the vascular apparatus, even in cases of severe bleedings, is such that great drops in hæmoglobin and red cell counts are unusual until many hours after the trouble has begun, and since the normal for the individual is generally unknown, any fall except a great one is of little immediate diagnostic aid. The estimations, though, should always be made, because every once in a while an unmistakable drop does occur and the case is clear. Besides, the leucocyte count might prove illuminating, especially in the obscure abdominal conditions.

Where the history would seem to indicate the possibility of hemorrhage, or where there is a known cause of bleeding, such as operation or an injury, the signs and symptoms enumerated in the previous paragraph

are considered classical, and a diagnosis of hemorrhage would be justified. One may go even further and say that in the absence of some of them, there are certain types of hemorrhage whose mode of onset is so typical that a diagnosis other than hemorrhage is almost inconceivable, although the possibility of error cannot be entirely overlooked. I refer particularly to those instances of ruptured ectopic pregnancy, where a woman previously well, in the child-bearing period, has a sudden sharp pain in her abdomen, faints, and on reviving, is prostrated. Hemorrhage is written all over her features. And the typhoid patient who suffers a sudden severe intestinal hemorrhage occasionally presents the same picture.

But what about those cases where other possibilities and probabilities come up for consideration? The post-operative cases that fail to react, or, reacting, slip away again; the sudden collapse of individuals, previously well, whose history is either negative or but faintly suggestive; the typhoid patient whose sinking spell may be due to perforation as well as hemorrhage, or to both, or to neither; the individual injured but evincing no evidence of his injury other than profound prostration? Where are our classical signs? They may be present in part, or *in toto,* and they may be just as eloquent as ever in proclaiming trouble of a serious nature, but no longer are they classical for

hemorrhage. These are the moments when a calm judicial mind is greatly to be desired.

If I were asked what one specific discovery would do the most good to the greatest number in surgery, I would almost unhesitatingly reply, "A pocket flash-lamp of such power that the inner workings of the human abdomen could be distinguished"—for it is the abdomen above all else that mystifies, and until the time comes when we shall actually be able to see what is going on, it will continue to do so. But we have no magic lamp, and the differential diagnosis of intra-abdominal conditions is at present so intricate and unsatisfactory and often based on evidence of such flimsy nature, that it really amounts to little more than a guess. Fortunately, however, intuition plays its part and the man who is more widely experienced, who is perhaps better seasoned by advancing years than his colleagues, and more used to reasoning things out, comes to have a sort of sixth sense that guides him to an interpretation more nearly correct than others reach—for certainly the signs and symptoms are apparent to all and are pathognomonic no more for him than for others.

I was once asked to see a woman, who had undergone a resection of part of her sigmoid, for a new growth, a lateral anastomosis being the means of uniting the severed bowel. The operation had been done

about eighteen hours before by Dr. John M. T. Finney in his characteristically thorough manner, and the woman had left the table in good condition and had continued to do well for twelve hours when, most unexpectedly, she had an alarming sinking spell during which she almost died. Her pulse became extremely rapid, breathing very difficult, and it looked very much as if there had been a temporary heart collapse for which the usual restoratives were promptly administered. They gave but little relief, however, and, as the patient's condition seemed desperate, a salt infusion was at once started, under the assumption that an intra-abdominal hemorrhage was in progress. This helped matters a little only, and still no signs of bleeding could be detected; drains had been placed through a puncture wound, but no blood showed on the dressings and their removal revealed none along the drainage tract nor within that area of the abdomen which could be investigated.

When I saw her the picture was certainly one of profound hemorrhage and shock. There were the rapid respiration, the rapid thready pulse, the pinched expression, the very low blood-pressure, and the cold clammy skin. The abdomen was soft. Blood counts were non-committal, as usually happens when they are most needed. But since no evidence of bleeding could be found in spite of repeated search, and the

woman was in the advanced fifties, I rather inclined to the diagnosis of broken heart compensation and advised against transfusion, for which I was consulted. Dr. Finney was at a loss for a diagnosis as were all others concerned, including one of the best medical consultants in the city. Thus matters hung for eight hours longer, during which time everything conceivable was done to revive the patient—all unavailing. At the end of this period the woman's condition was so critical that, under the assumption that an intra-abdominal catastrophe of some nature surely had occurred and was responsible for the trouble, it was decided to reopen the abdomen and look in, a preliminary transfusion being done in order to prepare the way. With the introduction of the first 100 c.c. of blood from her son, a slight improvement took place, but as further improvement failed to follow the second 100 c.c., the transfusion was temporarily stopped. Dr. Finney was just preparing to open the wound when the patient died. I thereupon opened it myself and discovered no blood at all, but a rather small amount of serosanguineous, thin fluid which under the miscroscope contained myriads of streptococci! And a streptococcus peritonitis had never occurred to one of us. Could anything be more baffling? An intra-abdominal catastrophe had truly occurred! There had been no cases of strepto-

coccus infection of any kind in the hospital for months and no cases of streptococcus peritonitis for over a year, and in these days of aseptic surgery a fulminating streptococcus peritonitis is an extremely rare occurrence. Here we had every conceivable sign and symptom of hemorrhage, of what is so glibly termed shock, and of heart collapse, and still not one of them was the underlying cause. The patient was profoundly shocked, it is true, but this was but the expression of the obscure cause. I confess that I was unaware prior to this that a streptococcus peritonitis could simulate these conditions. Since then I have seen one other similar case, also post-operative, and for which I was summoned to do a transfusion for bleeding. I diagnosed this one correctly. The patient died four hours later, twenty-four hours after the operation, and my diagnosis was confirmed. Differential diagnosis is extremely difficult and experience is a great asset.

I mention heart collapse as a possible obscuring element in the interpretation of seeming hemorrhage because of another most instructive mistake made two years ago. Ordinarily a sudden break in heart compensation is recognized by an alert physician without great difficulty, and the diagnosis of hemorrhage is rarely complicated by the suggestion of this as a possibility, but late one night I was hurriedly called to the

hospital to see what was considered an alarming case of concealed intestinal bleeding in a young woman who had been running an ordinary typhoid course. While using the bed pan, the patient had suddenly suffered a most alarming collapse, the chief manifestations being loss of consciousness, extreme pallor, rapid pulse and apparent shortness of breath. Prompt restorative measures were instituted with some success, but the condition remained quite alarming and, all things considered, a diagnosis of concealed typhoid hemorrhage seemed proper. The hæmoglobin and red counts were made, but as usual could not be relied upon as true indicators. A more reliable index of probable bleeding seemed to be the blood-pressure, which was only 90 mm.

Before I arrived, strophanthin had been given and an infusion of 700 c.c. of salt solution which had been taken up with slight, but not marked, improvement. There had also been a consultation between the patient's physician, a man instructed in all branches of medicine, and one of the leading consultants of the city, both of whom had gone over the situation in their usual painstaking manner, and had ruled out heart collapse in favor of hemorrhage.

To me the picture was typical, so I warned against further infusions, fearing that renewed or prolonged bleeding might be encouraged by filling up the vessels.

But it did not seem to any of us that the patient was in imminent danger; to be sure a blood-pressure of 90 mm. is near the danger line, but a low pressure and a slowed circulation is to be desired in cases of obscure intestinal bleeding. We decided to watch the patient most carefully for evidences of further bleeding, meantime preparing for transfusion by having the tests made for prospective donors.

By morning the patient was slightly improved; the pulse was a bit slower and the blood-pressure about the same. We waited, and by evening we decided to wait still longer. *We are still waiting to see the slightest evidence of any bleeding.* There were no further disturbances, and the patient ran the typical typhoid course from which she made an uninterrupted recovery.

Looking backward, it seems that the lack of any marked abdominal distress or muscular rigidity might have put us on our guard, but abdominal hemorrhage is not always accompanied by marked physical signs. Then, too, it hardly seems likely that an embarrassed circulation could take up with apparent avidity 700 c.c. of salt solution without becoming still further embarrassed, and this did not happen—possibly as a result of the supportive strophanthin. We considered, at the time, the possibility of an ulcer having perforated with the resultant peritonitis and shock and possible intra-

peritoneal bleeding, but the abdominal examination appeared to eliminate this and no sign or symptom of peritonitis appeared subsequently; so we are forced to the conclusion that we were dealing with a pure case of heart collapse that so nearly approximated a concealed intestinal hemorrhage as to render differential diagnosis impossible.

We do not know exactly what shock is; in fact, we have no standard conception of it other than that it is a condition of lowered vitality, the index of which is a semiconsciousness, a relaxation of practically all the organic faculties, and a blood-pressure of minimal limits, to say the least. Such a state could hardly come about except through an accident of violence or as an accompaniment or result of some other condition, such as hemorrhage, perforated ulcer, *et cetera,* so that pure shock as such rarely has to be eliminated—with perhaps one exception, namely, following a dangerous and prolonged operation. Loss of blood during operation, peritoneal irritation or manhandling, violence in reducing fractures, prolonged, carelessly given anæsthesia, all these factors not infrequently prove too much of a burden, and the so-called postoperative reaction and return to consciousness is delayed or fails to occur—or the reaction and consciousness may appear only to be accompanied or followed by a lassitude which progresses, in spite of proper

treatment, to an alarming collapse. Is this hemorrhage? shock? or both?

The type of operation, the operative methods involved, the whole operative program studied from every angle will occasionally give the clue to the trouble, although I am rather of the impression that nowadays, almost all surgeons are quite careful of their hæmostasis for the simple reason that they have gotten into difficulty at some previous time as a result of carelessness or have seen the consequences of it in others. Still there are many quite remiss in those little refinements, such as deftness, recognition of rights of tissues, *et cetera,* which go to make the finished operator. However, the surgeon's skill taken for granted, I should incline toward a diagnosis of shock rather than post-operative hemorrhage, unless the bleeding can be demonstrated, or there has been some definite reason to suspect it. Delayed return to consciousness is not uncommon after operation and certain individuals seem more sensitive to mechanical manipulations than others, factors to be borne in mind. The safest way to estimate these patients is to sit by the bedside and study every feature connected with the case over a considerable period of time, taking blood-pressure readings at frequent intervals and making blood counts at definite periods of every half hour. A persistently diminishing blood-pressure and

decreasing blood count, with no improvement in symptoms in spite of proper treatment, would indicate hemorrhage or at least warrant an investigation of the operative field.

An acute pancreatitis is usually accompanied by a state of such profound collapse and such rigid abdominal walls that hemorrhage is hardly to be considered, and a perforated gastric ulcer belongs in the same category, in addition to having a history which, if obtainable, is usually sufficient to point the way to the probable diagnosis. Both conditions demand, and usually receive, immediate operation, with the clarifying of any diagnostic doubt. I mention them in this connection because they must be kept in mind in any consideration involving the abdomen, but I have never had occasion to do a transfusion in the initial state of either condition. It is conceivable, of course, that a good sized vessel may be eroded at the site of perforation—indeed, cases are on record where this has happened—but as a rule this does not occur. Furthermore, it is also true that the vast majority of those gastric ulcers that do bleed do not perforate—at least not at the time of the hemorrhage. The possibility of this condition and that of acute pancreatitis is merely to be borne in mind as a possible eventuality where there are strong grounds for suspecting hemorrhage.

The blood findings in cases of acute hemorrhage

are peculiar to say the least. The red cells are supposed to fall in number, the hæmoglobin is also expected to fall, while the white cell count is supposed to rise; as a matter of fact, they do act as scheduled in many cases, but the instances in which they do not are so frequent, that unless serial readings are taken little dependence is to be placed on them. In 1909 Crile reported eighteen observations on the hæmoglobin and red cell changes in donors after transfusion. There was a fall in the red cells seventeen times out of the eighteen, but in five instances the fall was very slight, while the hæmoglobin fell twelve times and remained unchanged six times. Of thirteen observations on the white cells, there was a rise in twelve, but it was slight in two of them, while in one case there was a fall. Several of the cases in which no fall could be detected, or in which it was very slight at first, showed distinct falls, some large, some small, a number of hours (seven, eight, or ten) after transfusion. And curiously enough the red cells and hæmoglobin do not necessarily correspond in their fall. In certain cases a definite decrease in the reds was noted, but the hæmoglobin decrease was so slight as to be of no significance.

It is therefore evident—for Crile's observations have been confirmed by everyone who has investigated the matter—that single blood examinations in

cases of severe hemorrhage cannot be taken too seriously. In the first place, the normal blood count varies within fairly wide limits with each individual, and it is extremely rare that the normal is known for the patient under consideration. When we add to this the fact that it is always extremely difficult to judge as to the amount of blood lost, one can readily see that the difficulties in this direction are practically insurmountable. Nor is it hard to understand why excessive blood losses need not necessarily be indicated by estimations made during or shortly after the hemorrhage, since it is well known that as blood flows out of its containing vessels, a compensatory involuntary contraction of the vessels takes place with a general narrowing of their lumen, thus giving more or less stability to the blood-pressure. The unshed blood remains undiluted in the contracted vessels and counts made during this period are consequently practically without value so far as revealing the true state of affairs is concerned. Not until the compensatory contraction of the vessels relaxes, can the surrounding tissue plasma pour into them, and as this usually does not take place till some hours after the hemorrhage, there *is actually* little or no blood dilution. It is true that there has been less blood all along, but there also has been *less blood-vessel lumen,* less actual space to be filled. When the relaxation does occur more space

needs to be filled, for which the actual blood is insufficient, so plasma is drawn in from the surrounding tissues to make up the bulk, and as plasma contains no cells, a count made at this time will show true depletion.

The differential diagnosis, then, between hemorrhage and conditions that simulate it, is a most delicate matter in many cases. Personally, I have never seen an out-and-out case of severe bleeding which had a high leucocytosis, so that I am accustomed to incline toward a condition other than hemorrhage, when this feature is found. At the same time, it has been unusual to encounter a leucocytosis sufficiently high to absolutely rule out hemorrhage in many of the obscure cases that have come under my observation for differentiation. Once in a while it is there, but not in the profound pulseless cases, as a rule.

I can only conclude this chapter with the reiterated advice to take a most careful history and to leave no test, laboratory or other kind, undone, and the suggestion that the countenances of patients who have suffered blood loss be studied. They come to have a look which, though not actually characteristically diagnostic, is different from the appearance presented by those whose condition is the result of something other than bleeding, a look truly gruesome and which I can best describe as cadaverously cyanotic.

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CHAPTER III

CONTROL OF HEMORRHAGE. FACTORS INVOLVED IN A DETERMINATION OF DANGER LIMITS. BLOOD-PRESSURE

THE control of bleeding, in general, is so well known and the means at our disposal for accomplishing this purpose are so uniformly used that detailed consideration need hardly be given each individual form. Pressure, the suture of lacerated tissues, the ligation of great vessels and the pack, are common elementary measures for attacking visible hemorrhages or those amenable to operative interference. But instances frequently arise where a successful outcome depends less upon actual mechanical measures than upon a keen judgment as to the time or the form of their application, less upon the actual cessation of bleeding than upon a prevention of its ever starting, and, finally, upon a coördination of efforts that involves, on the one hand, the most painstaking investigations as to cause and, on the other, a broad comprehension of the many factors concerned with blood loss and blood coagulation.

The intensive study of hemorrhage has really been neglected up to the present time and for the very good reason that no special purpose could have been

served by a deeper knowledge of its workings. Until the advent of blood transfusion in a practical form, there was no dependable reserve remedy in the physician's armamentarium so far as great blood losses were concerned and many features connected with the phenomenon of bleeding stand out in the high light of present-day knowledge that were quite obscure not very long ago. Chief among these is the amazing futility of drugs and next in order is the abuse of salt solution.

One has only to consult the hospital records of a few years ago to discover how profoundly drugged were most patients who had the misfortune to bleed, and a little closer study of the same records will show how thoroughly water-logged by salt solution they were, in addition. That any truly serious hemorrhages were successfully combated is a wonder, and that more fatalities did not occur speaks rather for nature's recuperative powers than for the medical man's skill and comprehension. The custom of drug therapy undoubtedly arose from a feeling of hopelessness in the face of intractable bleeding and the necessity of doing something in a losing fight, while the salt solution therapy was a later development consequent upon the discovery that many individuals whose bleeding had been stopped before it progressed too far could be saved by this means. That it had its limits and was

capable of doing great harm did not become apparent till rather recently.

Morphine judiciously administered is of distinct benefit in quieting a restless patient and in stilling active peristalsis where intestinal bleeding is in process, but its indiscriminate or continued use is to be avoided, because, in the first place, a false security may be brought about, and, in the second place, the large or cumulative doses tend to lower the blood-pressure, a distinct harm oftentimes because the bleeding itself brings this about, and minimal limits are dangerous and undesirable. Stimulants like strychnine, camphorated oil, atropin, digitalis, strophanthin may possibly steady a faltering heart, but it is well to remember that the heart is not the cause of the bleeding, and any irregularity is liable to be due to causes other than the heart itself.

Ergot and pituitrin doubtless have their places in ordinary obstetrics, but once a uterus has become atonic to such extent that bleeding has become serious enough to require packing, I have rarely seen either of them be of further service, although I have seen repeated injections of one or both given. It may be that the atonic condition came about *because* they failed to do their work in the first and usual instance. That we have no means of ascertaining, but certain it is that later on they do not seem to help matters.

In the same category may be placed the various sera. Cases are on record where rabbit serum has checked bleeding of a really serious nature. I know of one instance where it did seem to stop a most dangerous post-operative general ooze from mucous surfaces in a deeply jaundiced patient, but I know of many cases where it utterly failed. And horse serum is in general equally valueless, although it is repeatedly given in many and various forms of bleeding. In a recent case of hemorrhage from a gastric ulcer six doses at from three- to six-hour intervals were totally unavailing. Even human serum is fast losing favor, although it certainly is more efficacious than animal serum. Held in high esteem in checking the bleeding of the new-born, melæna neonatorum, it has of late been found sadly wanting. Only a few months ago, in one of my cases 15 c.c. were given at the first sign of bleeding, with no effect whatsoever. It does help occasionally, but too much reliance cannot be placed upon it. Tissue extract and fresh human tissue are of certain service if applied directly to bleeding surfaces, but the field for this is decidedly limited. Calcium lactate need hardly be mentioned. It is of no use once bleeding has started, and as a prophylactic it is of doubtful value.

As a general rule, a quarter grain of morphia is indicated at the start of any hemorrhage to quiet the

restlessness; after that the doses had better be smaller because of the depressant effect of this drug on respiration and blood-pressure. Measures to stop the bleeding should be instituted immediately, the body should be kept as warm as possible, the foot of the bed elevated, the limbs bandaged if it seems advisable, the patient kept quiet and fluids given *ad libitum,* liquids of any and all sorts, by mouth, per rectum, subcutaneous infusion, intravenously—coffee, tea, water, salt solution, ice—anything at all that will quench the intolerable thirst and keep up the bulk of the circulating medium—*all within reason.* And here, perhaps, I may be permitted to sound a note of warning—too much has been expected of salt solution. The custom of giving salt solution (or water) per rectum after an operation of any magnitude is a good one and the salt infusion in cases of bleeding is also good, as is, at times, intravenous salt—*all within reason.* But it is ridiculous in the extreme to keep filling a patient full of salt solution just because a great quantity of blood has been lost. Salt solution will not turn into blood, yet it is all but expected to do so.

If I have seen one, I have seen a dozen patients actually waterlogged by salt solution, and with no improvement whatsoever. It never seems to occur to some men that a heart can be overdistended, that the blood can be made too dilute, that if 1000 c.c. or

1500 c.c. of salt solution do no good, a greater amount will be equally valueless. But time and time again I have seen infusions repeated after 2000 c.c. of salt have been taken up without any benefit at all. Everyone knows it is proper to give salt solution in cases of blood loss, but very few stop to consider how much ought to be given. Some three years ago I was asked to see an old gentleman of sixty-five who had had a suprapubic prostatectomy done. He went off the table in very good shape, but a few hours later began to bleed and had to be repacked. Even this did not stop the ooze, so about four or five hours after the operation he was taken to the operating room and thoroughly packed under light gas anæsthesia. Rather shocked from this procedure but still in fair condition, he was returned to his bed and readily took up 2000 c.c. of salt solution. In spite of this he gradually became weaker and finally developed a Cheyne-Stokes form of respiration. When I saw him his blood-pressure was around 70 mm. and he was in a semiconscious condition. Those in charge wished to delay because he was taking up the fluids so well, but gave in after a brief argument. On incising his arm for a direct transfusion, not a drop of blood flowed from his tissues, but clear serum (salt solution) flowed very freely. The introduction of a few hundred c.c. of blood from his son saved his life; and curiously enough the Cheyne-Stokes

form of respiration disappeared while the blood was actually flowing into him.

It should be generally understood that if the bleeding has not been too great a few hundred c.c. of salt are all that is needed to tide a patient over a dangerous period. In cases of very severe hemorrhage the amount might be increased a bit, but if 1000 to 1500 c.c. do not steady a falling blood-pressure or cause a slight rise, its introduction had better be discontinued. Even where there has been a rise, the greatest caution must be exercised, for be it remembered that in these desperate conditions salt solution will frequently cause a rise in blood-pressure but will *not* sustain it. Where the bleeding has been excessive, a transfusion of blood is indicated because it has been conclusively shown that blood alone can raise a pressure and sustain it. Salt solution has no sustaining power *per se,* and when the fall comes after a rise from this means it usually portends the end, for added salt solution is useless. *It never raises a pressure twice!*

As the result, then, of blood transfusion, we have been able to really study the phenomenon of hemorrhage for the first time, and we have learned the value of doing as little as possible in the condition. Rest, quiet, attempts to check the bleeding by mechanical means, an ice-bag over or as near to the site of bleeding as possible, a bit of morphine for the restlessness occa-

sioned by the condition, and salt solution and we have the entire armamentarium for treating bleeding. For we have learned that the body itself does more toward checking hemorrhage than can be done by outside means, by automatically lowering its own blood-pressure and thereby causing a slowing of the circulation and renewed opportunity for coagulation of the blood at the site of leakage. But the more I see of hemorrhage and anæmia in general, the more am I convinced of the utter futility of having a specific rule by which to be rigidly governed. Each case is a study unto itself, each individual represents an entity which must be judged from all angles, and experience in the condition must have a great deal of weight in the ultimate decision as to the course to pursue. It is advisable, though, to have some tentative plan of procedure in cases of hemorrhage, and, since there are certain fundamental features common to a degree to all cases, it is possible to formulate a working rule. For instance, a sudden loss of blood is a much more serious matter than a gradual depletion and a rapidly falling blood-pressure is always a warning of value, though it must be remembered that nausea of the slightest degree will affect this phase of the situation. But these two features really are dependable in the majority of instances and experience has demonstrated that a good working rule is to transfuse if the blood-pressure falls

as low as 70 mm. of mercury, since life is hardly possible with anything below this limit. In some instances, if the physician or surgeon in charge of the case has not taken the steps usual in emergency cases it may be wise to delay until these can be instituted—preparation for transfusion being made in the interval. If the actual bleeding has been checked, if the patient is quiet, if salt solution has been given in the proper manner, and the blood-pressure still remains around 70 with the tendency to flutter a little below this point, it may be assumed that the case is utterly hopeless, unless new blood is introduced; and procrastination at this stage of the game is a fearfully dangerous plan, as the following story illustrates:

In the Fall of 1915 I was called to see a woman who had had a placenta prævia, and had been delivered in the manner usual for such conditions, a large amount of blood being lost, though not nearly enough, according to the obstetrician in charge, to have caused the terrific shock that ensued. The usual measures to combat such a condition had been carried out before I reached the hospital. When I first saw her, the patient was in a semiconscious condition, breathing was very shallow, her pulse very rapid, and her pressure around 70 mm. The obstetrician in charge of the case, however, felt that in the fifteen minutes prior to my coming there had been a slight

improvement, and the blood-pressure readings appeared to corroborate this, so that it seemed as if the condition might be due more to shock than to hemorrhage, and that if left alone the patient might recover without transfusion. We waited just a half hour, but during those thirty minutes we lost our only chance, for suddenly the blood-pressure dropped still further, the patient became absolutely unconscious and died just as the transfusion was started.

But we must not fall into the habit of adhering too closely to the blood-pressure for guidance, because it is not absolutely constant and at times, in cases of extreme danger, it never reaches the lowest level, or at least it never reaches that until actual exitus is imminent. For instance, in September, 1916, I was asked to see a man who had been bleeding from an obscure intestinal condition for over twenty-four hours. He had passed tremendous quantities of blood and looked quite ill, yet his blood-pressure reading when I saw him was 136 mm. Being a man of fifty-one, that was, perhaps, a little low, but no one who has a pressure of 136 mm. is in any danger of dying from brain anæmia under ordinary circumstances. And another curious feature of this same case was that his hæmoglobin registered 68 per cent. No better illustration could possibly be had of the points I have been making in this chapter than this single case. The question arose as to what to do. He had been

given horse serum repeatedly with no apparent effect on the bleeding, and, while he looked quite ill and those in attendance felt that he was almost surely beyond help, I could not feel that he was in any imminent danger and therefore decided to study the case further, in the meantime testing out donors in case transfusion should become necessary. Two hours after I first saw him he had another huge hemorrhage from the bowel and his pressure dropped ten points while his hæmoglobin dropped eight points. The man at this time looked desperately ill, and in spite of the fact that he had a blood-pressure well within the usual limits of safety and a hæmoglobin quite well up in the schedule, I decided upon and carried out an immediate transfusion. From the moment blood was introduced the patient's condition improved and he never bled another drop. His subsequent history has revealed the fact that the condition was a duodenal ulcer.

A survey of the foregoing pages leads one to the conclusion that many considerations enter into a determination as to the wisest course to pursue in controlling severe bleedings. Conservative tactics are in order so long as actual danger limits are not in evidence, but it has been conclusively shown that one must be most guarded in concluding that this point has *not* been reached, since all signs may be deceptive

and a false security may have come about through the unwise use of ineffectual drugs, especially opiates. It has been further demonstrated that the use of salt solution in all conditions of hemorrhage is most helpful if care is exercised, but that its indiscriminate employment is fraught with grave danger and frequently results in taking away from the patient what little chance he may have had by over-distending the heart, over-diluting the blood or actually waterlogging his tissues. But a working rule has been suggested based upon the two features most dependable and constant in dangerous hemorrhages—namely, the rate of blood loss and blood-pressure readings, a base line of 70 mm. of mercury being assumed as an indication for immediate blood transfusion regardless of all other features of the case.

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CHAPTER IV

INDICATIONS FOR TRANSFUSION

In the early days of transfusion, when it was a real ordeal to accomplish the blood transfer, indications for the procedure were limited practically to hemorrhages of the most exsanguinating variety and to anæmias of such grade that recovery or improvement without added blood was utterly impossible. But the technic of the operation has undergone a gradual evolution until now it is so uninvolved, so readily accomplished, that its field of usefulness has broadened enormously and bids fair to spread still further, and now transfusions are carried out where there are no true indications at all, strictly speaking, the mere possibility of benefitting a condition by the addition of blood being considered sufficient warrant. In other words, transfusion of blood was used formerly purely as a life-saving means, a heroic last resort, while now it not only fulfils this purpose to an even better degree than formerly but has taken on the added importance of therapeutic usefulness, which at once opens up possibilities and opportunities heretofore inconceivable.

Any absolute tabulation of indications under

present-day conditions when transfusion is still in a process of evolution must be taken as subject to revision, as the future will very likely see its use in maladies not at present under consideration and its disuse in conditions for whose relief it is now employed. Furthermore, it must be understood that *absolute* indications do not exist for transfusion in the same sense that they do for other surgical procedures such as, for example, an appendectomy for an acute appendicitis or a radical amputation of the breast for a carcinoma. The reason for this is that many times a transfusion is done for a phase encountered in the course of some acute or chronic illness rather than for the elimination or relief of some definite pathological entity, and since this phase amounts to a depletion of the circulating medium of the body resulting from accident or disease, no absolute indication can be possible because of our inability —at the present time—to determine actual limits of blood loss. We may say that the introduction of blood is indicated in all exsanguinating hemorrhages, but in making such a statement it must be understood that there is an implied reservation, for one must be able to judge which hemorrhage of the exsanguinating variety will prove fatal without transfusion, since the term exsanguinating is used rather loosely and does not always indicate a fatal hemorrhage.

This distinction between indications for transfusion and for certain other operations may seem more fanciful than real, but one has only to engage in the work for a brief time to realize its truth. There can be no more difficult problem at times than a determination as to when a transfusion is or is not indicated, nor can a more embarrassing or dangerous situation arise than where an honest difference of opinion exists between medical advisers, with the patient's life hanging in the balance. The oft-repeated saying that the public ward patients fare best because they do not suffer from prolonged consultations between a number of medical advisers is especially applicable in transfusion work; their condition is sized up with as little delay as possible and the proper measures for relief are instituted at once, while there is a tendency to delay matters in the case of the so-called private patient.

Obviously it would be unwise to transfuse all patients who have suffered a terrific hemorrhage, because the majority of them recover without it. A somewhat similar state of affairs exists with regard to other conditions, such as, for example, hæmophilia, melæna neonatorum, bleeding from jaundice, *et cetera,* though in a different way. Transfusion would probably stop the bleeding in nearly every case and one might conclude that it is therefore indicated, but there are other measures which are sometimes indicated

prior to transfusion, such as the injection of serum or the subcutaneous injection of whole blood or the use of calcium. So that the question of indication is a complex one for not alone must one decide as to whether or not the procedure is indicated, he must further determine *when* it is indicated. If a severe traumatic hemorrhage is under consideration and certain operative measures must be carried out, those in charge of the case must be able to decide as to whether the transfusion should be done prior to them, during their course, or afterwards. Or if an infant is suffering from melæna neonatorum, it will not suffice to say that transfusion is indicated but the serum treatment should be tried first just because injected serum will stop the bleeding in a certain proportion of the cases. It may be that the case in hand has progressed too far, that simple cessation of the bleeding is not enough and therefore transfusion should be done without preliminary serum treatment in order to accomplish the double purpose of stopping the bleeding and combating the profound anæmia.

Hard and fast rules cannot be drawn. One must be guided by the single purpose of doing the most good with the minimum of risk. If a difference of opinion exists as to the advisability or necessity of a transfusion, it is best to postpone the operation if the patient is in no imminent danger, because the re-

cuperative powers of the human body are such that many recoveries come about unaided in conditions that seem hopeless at first sight. On the other hand, a patient in imminent danger ought not to be subjected to unnecessary delay. I hardly think that any great number of unnecessary transfusions are carried out, but I am convinced that many cases are lost either by not transfusing at all or by doing it too late. And not only this, there are many, many cases whose illness could be materially shortened by the introduction of blood, whose operations could be made less hazardous, whose whole after-course could be made less burdensome.

With this preliminary survey, then, it seems warrantable to formulate the following list of probable indications[1]:

I. *Transfusions for actual hemorrhage:*

(*a*) Traumatic.

(*b*) Gastric and duodenal ulcer.

(*c*) Post-partum.

(*d*) Ruptured ectopic pregnancy.

(*e*) Typhoid hemorrhage.

II. *Transfusions in connection with surgical operations:*

[1] I have followed very closely the classification of Libman and Ottenberg, as given in the reference appended at the back of the chapter.

(*a*) Preliminary to, during or just after operation.

(*b*) For post-operative hemorrhage.

(*c*) For post-operative shock.

(*d*) For post-operative anæmia and prostration.

III. *Transfusions for the relief of hemorrhagic conditions:*

(*a*) Purpura hemorrhagica.

(*b*) Hæmophilia.

(*c*) Hemorrhages secondary to (1) blood diseases, (2) severe infections, (3) jaundice, (4) idiopathic uterine.

IV. *Transfusions for blood disease:*

(*a*) Pernicious anæmia.

(*c*) Leukæmia.

V. *Transfusions for infections:*

(*a*) Infections with pyogenic organisms.

(*c*) Subacute streptococcus endocarditis.

(*d*) Subacute infection of any nature other than septicæmia.

VI. *Transfusions for intoxications and poisonings:*

(*a*) Toxæmia of pregnancy.

(*b*) Eclampsia.

(*c*) Uræmia.

(*d*) Benzol poisoning.

(*e*) Illuminating gas poisoning.

VII. *Transfusions for debilitated conditions:*

(*a*) Cancer.

(*b*) Malnutrition.

(*c*) Simple anæmia from any cause.

Subsequent chapters will consider these various conditions in detail.

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CHAPTER V

DANGERS OF TRANSFUSION. HÆMOLYSIS AND AGGLUTINATION

That quite a few lives have been lost through transfusion cannot be denied, but that most of the fatalities have resulted from inexperience and occurred in the early days of the procedure is equally true. In reviewing the statistics on this work, it must be remembered that certain of its most important features have come to be clearly understood only within the last few years, and that its results are sometimes influenced by the extraordinary circumstances under which much of it must be carried out.

In 1914 I sent out a questionnaire to twenty men who were actively engaged in transfusion work, asking for their opinion and experience in regard to its dangers. This was done in order to be able to set before the profession the absolute facts in a matter that had hitherto been dealt with only in generalities, in spite of the fact that accurate knowledge was of prime importance. From the fourteen replies, the following facts were deduced: In 800 transfusions there occurred fifteen cases of macroscopic hæmoglobinuria (an incidence roughly of 2 per cent.) with

eleven recoveries and four deaths.[1] Six of these transfusions were done for tuberculosis, no deaths; two for post-operative hemorrhage, one death; and one for hæmophilia, no deaths. In three of the deaths, no hæmolytic tests were made, although there was plenty of time to do so in two of the cases, the conditions being lymphatic leukæmia and pernicious anæmia. The third case was an extremely hurried emergency, my own case. In the case of the fourth death, tests were made, and it was known prior to operation that "the donor's cells were slightly agglutinated by the patient's serum." But it was necessary to use this donor because no other was available, and since agglutination is an entirely different process from hæmolysis—which was negative in the tests—it was evidently considered safe to use the donor under the circumstances. A similar predicament arose in my second case, in which tests revealed slight hæmolysis (no agglutination) of the donor's corpuscles by the serum of the recipient. No other donor was available and the transfusion seemed most desirable, even essential to the success of an exploratory operation and pyloroplasty in a man almost exsanguinated from a bleeding gastric ulcer. Besides, I had been under the impression from

[1] One of the men who failed to answer reported in the *J. A. M. A.* for March, 1914, a series of 135 transfusions with three instances of hæmolysis. All three cases recovered.

statements from various sources that hæmolysis *in vivo* did not necessarily follow its occurrence *in vitro.* Perhaps this is so, but I will never again take any unnecessary chances. This patient had a well-marked hæmoglobinuria within twelve hours after transfusion, as a consequence of which he suffered a marked fall in hæmoglobin, losing practically all the blood we gave him. His recovery is probably due to the fact that his serum was only very slightly lytic, and that, knowing the danger we ran, we transfused a minimal amount of blood—just sufficient to tide him over his operation. Whether he really derived any benefit, in view of his hæmolysis, is a debatable question which need not be considered here.

Proceeding with the study of these fifteen cases of hæmolysis, in the eleven recoveries, tests were made in nine instances and hæmolysis prognosticated, evidence quite sufficient to indicate the value of tests when properly made. That there were no fatalities in these nine instances is a purely accidental circumstance. In one other instance besides my own, the patient's serum was lytic to donor's cells—that is, the patient's serum simply destroyed the red cells introduced into the circulation. The exact test contraindication was not mentioned in the other seven cases, but in the two mentioned it must be assumed that the patient's recovery can be ascribed to the fact that, since the foreign cor-

puscles alone were destroyed, a quantity of them, insufficient to cause death when broken up with the resultant liberation of their hæmoglobin, was introduced at transfusion. Had conditions been reversed—that is, had donor's serum been lytic to recipient's corpuscles or, in other words, had the patient's own corpuscles been liable to destruction—there would have been, in all probability, two more deaths to chronicle.

So long as the whole blood was used the method of transfusion employed, direct or indirect, appeared to be immaterial. In the list of indirect transfusions, however, there were about sixty in which defibrinated blood was used. One sudden death resulted in this series, and I have knowledge of one other death (not reported) from a similar cause. It seems that the use of defibrinated blood introduces into transfusion a factor that does not occur when the whole blood is used. This factor is both obscure and dangerous, and since the transfer of whole blood is even simpler than that of the whipped variety, I have been at a loss to understand why any one should persist in employing the latter. Prejudice or habit may be the cause, but the patient's welfare, at least, should be shown some consideration.

There were six fatalities due to causes other than hæmolysis, four from acute dilatation of the heart and two from questionable anaphylaxis.

Seven of the surgeons considered hæmolysis to be the chief danger of transfusion—one man volunteering the information that he personally knew of three unpublished deaths from this cause. One considered this the second chief cause, while two saw no danger in it under any circumstances and made no tests! Three men regarded acute dilatation of the heart as the chief danger, while four looked upon this as the second chief factor, six disregarding it entirely. One man considered embolism the chief danger, and one sepsis, because frequently the operation must be hurried.

Of course, we are all more prone to report our successes than our failures, so that a considerable number of accidents and fatalities in the course of transfusions must be reckoned as having occurred without being reported. I personally know of several, and verbal reports of others have been brought to my attention; but further experience in the work, and communication with colleagues have convinced me that the above report still remains approximately correct. If anything, an improvement in results can be counted on, because with the diminishing popularity of direct transfusion, the danger of overdistention of the right side of the heart coincidently has decreased, and with the more general knowledge of the latent possibilities of hæmolysis and agglutination, labora-

tory tests for matching up bloods prior to transfusion have become the rule rather than the exception.

The only two features that may possibly keep the average accident mortality figures where they were or raise them a bit, are, first, the more widespread use of transfusion by the profession at large and the consequent inexperience of many operators and, second, the recent practice of adding chemicals to the blood in order to retard coagulation. Time will doubtless remove both of these complications, but an unbiased view compels the recognition of certain accidents and deaths that have necessarily occurred in the development of the recent and promising citrate technic of transfusion.

What, then, do we mean by dangers of transfusion and how may they be recognized and avoided? To consider them in their logical order, an overdistention of the heart can occur only in one way—inflow of a liquid whose pressure, rate and volume are greater than can be cared for by the right ventricle of the heart, and this can occur when the fluid is running in of its own accord, as in a direct transfusion or an ordinary intravenous infusion of salt solution, or when the liquid is being injected by needle and syringe. It is an ever-present danger that can be avoided only by constant watchfulness on the part of operator and assistants, for it must be remembered that in practically every instance of transfusion, the blood pressure

of the patient it quite low—usually much lower than normal—so that the pressure of the inflow must be regulated accordingly, that is, it must be a little, but not too much, higher than the intake side.

Hearts vary, too, quite markedly in their ability to accommodate an unusual inflow. A young individual who has been depleted by an accidental hemorrhage will almost never be embarrassed by a rapid inflow of salt solution or blood because his heart muscle is young and strong and capable of standing almost any strain, but the heart of that same young man would be able to stand very little had he been through a long typhoid struggle during the course of which an intestinal hemorrhage necessitated the introduction of blood. The man or woman of fifty or sixty whose heart has undergone myocardial changes must always be watched most carefully. Further, we must keep in mind the fact that transfusion is not infrequently done nowadays for the relief of conditions such as pernicious anæmia, where the trouble is apparently only with the cellular element and the fluid content of the blood is approximately normal. Under such circumstances, with the vessels filled to practically their normal capacity, an embarrassed circulation can only be avoided by a most circumspect injection of liquid of any kind.

The signs of an overdistended right heart need not

be unduly dwelt upon, since they are none other than those of a broken heart compensation, and as such are familiar to all medical men. The slightest nausea in the course of a transfusion should serve as a danger signal; blueness of the lips or skin is an added warning, as is a cold clammy skin upon which beads of perspiration break out. Given in addition shortness of breath, a rapid, irregular pulse and vomiting and we have a classical picture of acute dilatation—one that should never, under any circumstances, be seen during the course of this work. At the faintest sign of trouble the inflow should be slackened and its pressure diminished and, if conditions do not promptly improve, the transfusion should be discontinued until the heart does recover, when it may be most gradually resumed.

So much for the patient who is awake or conscious. For those who are anæsthetized or are unconscious from shock or any cause that necessitates transfusion, the matter becomes more complicated, since there remain for guidance only the pulse, color, and respiration. In these cases a stethoscope strapped to the precordium is perhaps the most trustworthy means of detecting early cardiac distress, but an alert anæsthetist can do much by constant watchfulness of respiration as well as pulse. The inflow of blood should be slower than usual and one should err on the

side of giving too little blood rather than too much under these circumstances.

It is possible, of course, to give a general infection in the course of a transfusion through faulty technic, and doubtless this has happened, but it has not occurred in my series of cases, and I am happy to say that no instance of it has come to my personal attention, although I have indirect knowledge of its occurrence. It should never occur, and, in view of the simplicity and rapidity of the present-day iodine technic made use of in preparing the skin for surgical intervention, only the grossest blunders could give rise to it.

The occurrence of an embolus during transfusion is recognized but is very, very rare. I have seen it once—during a direct transfusion—at least, in one of my cases signs arose which could be attributed only to an embolus; but since the patient recovered I was unable to prove it. Theoretically, instances of embolism ought to be of rather frequent occurrence, but one hardly ever sees this danger even mentioned. I do not recall seeing a single report of it in the literature, but have heard of one case which recovered. It would seem that clots which occur in needles and tubes during transfusion are not friable and that bits of them do not tend to wash off, as might be supposed. When clot formation begins, it adheres firmly to the side of the tube or needle and either remains there or increases

in size till it occludes the lumen, and everyone knows how difficult it is to free the lumen of the smaller needles from a blood-clot. It takes an enormous amount of pressure, in fact the pressure that one can get from a 20 c.c. record syringe hardly suffices, and a solid piece of wire must usually be brought into play to get the desired result. This is probably the reason why emboli do not occur.

The danger of transmitting disease by transfusion is real but fortunately small. Syphilis is about the only one that need be feared and if careful tests are made prior to transfusion, as should be done, this danger can be entirely eliminated. It occasionally happens, though, that time to do the tests is lacking or there are no facilities, in which case careful physical examination and the history must be relied on. I have positive knowledge of one case where a son transmitted an acquired syphilis to his father who was suffering from pernicious anæmia. The boy evidently knew he had the disease, because he refused to have his Wassermann done while there was time. The father finally took a sudden turn for the worse and an emergency transfusion was done from his son—with disastrous consequences. This is the only instance of this that I know of, but since its occurrence, I have insisted on a Wassermann in every transfusion not of an emergency character, whether the donor is a relative or

not, and in the emergencies I try to rule it out as best I can, explaining the danger to the relatives.

I have once transmitted a double infection of malaria by means of a transfusion, the types being that of tertian and æstivo-autumnal, and have knowledge of one similar occurrence which has not been reported in the literature. In fact, I have never seen a report of this sort in all the voluminous literature on the subject of transfusion and had never considered this as a possibility, since it had been my impression that the mosquito was a necessary intermediary in the transmission of this disease. Since the undoubted occurrence of my own case, however, I have learned that certain Italian workers have successfully transmitted the disease by blood injection not once but several times. My case occurred early in 1917 and is unreported at the present writing, but the details will be given very shortly.

After all is said, the only real danger in blood transfusion is that resulting from hæmolysis and agglutination, either one or both combined, although, of the two, hæmolysis is far the more frequent in occurrence and the more dangerous. By hæmolysis is understood the destruction of red blood-corpuscles, a pathological phenomenon that always occurs when bloods of different species are mixed and one that may or may not come to pass when two perfectly normal bloods of

the same species are mixed. Its exact cause is unknown, but in the case of two humans the serum of one may destroy the corpuscles of the other with the consequent setting free in the blood stream of the hæmoglobin contained in them, the index being a hæmoglobinuria, since the liberated hæmoglobin is excreted by the kidneys. A very mild grade of hæmolysis probably occurs every time a transfusion is done because there must be a certain minimal cell injury and destruction in the actual handling and transfer of the blood no matter what method is used or how great the care, for blood cells are so delicate that even momentary contact with a foreign substance like a tube or needle must injure them. But these grades are of no significance as far as is known, since they never give rise to symptoms and never cause a microscopic or macroscopic hæmoglobinuria. Possibly spectroscopic tests would reveal the presence of these mild grades, but since they are harmless they will not be considered.

The grosser grades, though, are of definite significance and usually manifest themselves shortly after the conclusion of transfusion, first in the shape of a chill followed by fever, and then by an alarming prostration of greater or lesser severity, depending upon the amount of blood destruction taking place. Hæmoglobin usually makes its appearance in the first voiding, being diagnosed by the reddish brown color of the

urine and a sediment like reddish brown brick-dust. If the case is a mild one the urine may be but faintly colored, and only one voiding may contain the hæmoglobin, as happened in one of my cases; but if severe and continued blood destruction is taking place the urine becomes progressively darker and the output diminishes as the kidney tubules become occluded by deposits of hæmoglobin in them. In a fatal case of mine, actual cessation of kidney excretion gradually took place, the patient becoming desperately prostrated and exhibiting all the signs of uræmia, from which she died.

It would seem to be impossible to stop the trouble once it has begun, but in one case I gave a 500 c.c. salt infusion the moment hæmoglobin made its appearance in the urine, and a prompt cessation took place. Whether this was because of the infusion or in spite of it, I am at a loss to say, but another recent case had an equally happy ending. Most likely the bloods in these two cases were only faintly antagonistic, but a salt infusion can do no harm, and, since no other means of combating the phenomenon has been suggested, it may be worth trying. *Prevention* by tests is of course the proper thing, but the first case in question had been tested and reported as satisfactory. Control tests showed them to have been faulty, the only serious error

of this nature I have encountered. Fortunately, the patient recovered.

Hæmolysis may occur in three ways: (1) *The red cells of the donor may be destroyed by the patient's serum;* (2) *the red cells of the recipient may be hæmolyzed by the donor's serum; or* (3) *the red cells of both may be destroyed by each other's serum,* an eventuality of the gravest sort. Naturally, if the patient's serum is hæmolytic to donor's corpuscles the degree of hæmolysis will depend entirely on two factors—first, the toxicity of the serum, and, second, the extent of the transfusion or the number of corpuscles introduced, because after they have all been destroyed the process must cease. If, on the other hand, the donor's serum is injurious to the patient's cell, the degree of hæmolysis depends solely on the toxicity of the serum; if it is strong enough there is no reason why it should not destroy every red corpuscle in the body. Naturally, if both sera are lytic, both the red cells introduced and the host's cells are liable to destruction in part or *in toto,* according to the lytic powers of the sera, one of which may be stronger than the other.

Thus the absolute necessity for preliminary tests must be apparent to all. When blood transfusion first came into vogue it was the common thing to poke fun at hæmolytic tests; many men had done numerous transfusions without tests and without the sign of

hæmolysis or other trouble, so that the feeling arose that its occurrence was a remote possibility and therefore one to be ignored. But it was not long before cases of hæmolysis began to make their appearance, and with the growing popularity of transfusion they became more and more common, until a number of fatalities had occurred and a distinct change of sentiment concerning the importance of the complication was noted.

The reason for this early false security undoubtedly was that the phenomenon of hæmolysis apparently does not necessarily take place in unlike or unsuitable bloods every time they are mixed, the explanation for this singular state of affairs being unknown. This has been proved by the fact that not once but many times bloods have been shown to be incompatible in test-tubes, but *in vivo,* in the body, no trouble has followed transfusion. The trouble is that one cannot predict the course of events and, since the vast majority of bloods that are incompatible in laboratory prove to be so at transfusion, the safest course to pursue is to rule out all donors whose blood shows the slightest antagonistic tendency toward the patient's blood, or *vice versa.* If several donors have undergone tests and all of them show incompatibilities and no other individuals are available for further tests, or if time is lacking in which to carry out further tests and if the trans-

fusion must be done, it is customary to choose as donor that individual whose blood appears to be most compatible. In general only a slight hæmolysis will follow *in vivo* where there has been slight hæmolysis in test-tubes; but one can never be sure, and the sense of insecurity is most disturbing. Furthermore, even slight hæmolysis is injurious to the kidneys besides being generally dangerous, so that I am accustomed to postpone transfusions until donors can be found who are absolutely suitable—unless delay is out of the question or there absolutely is no possible way of securing other donors. Never will I forget the case where a wife was a husband's only possible source of blood, and he needed it badly. In spite of the warning tests, which, however, indicated only slight incompatibilities, I did the transfusion. A violent hæmolysis resulted and certainly undid all the temporary good the new blood had done. Fortunately, the condition was shortlived and the patient recovered, but his prostration while it was going on was profound, and he certainly looked as if he could not survive.

Where the bloods are truly compatible the post-operative course of a transfusion is so smooth. There is no sign of a chill or other discomfort except sometimes a feeling of fulness. The temperature hardly rises above normal and there is so often that most to be desired feeling of well-being on the part of the

patient. All the chills, the high fevers, the nausea and vomiting, restlessness, *et cetera,* occasionally met with must surely be the result of incompatibilities, since they rarely occur where preliminary tests have been accurately done and compatible bloods used.

The phenomenon of agglutination, by which is understood the clumping of red cells, is apparently much less dangerous to life than hæmolysis, but is of much more frequent occurrence. It has been shown by Moss that agglutination frequently occurs without hæmolysis, but hæmolysis is always associated with agglutination or preceded by it. This knowledge is most useful in carrying out appropriate tests for hæmolysis and agglutination.[2] I have never encountered any trouble from it in my own work nor have I ever seen any, although an apparently authentic case of sudden death from agglutination occurred about one year ago at the Johns Hopkins Hospital. In this instance the appropriate tests had been carried out, but shortly after transfusion was begun sudden exitus took out, out of a clear sky. The operator was so nonplussed at the unexpected turn of events that he immediately undertook a search for the cause, during the course of which numerous blood smears were taken which showed nothing but clumped, agglutinated red cells, the clumps being of all sizes. Evidently the two

[2] See Appendix.

bloods had been so markedly agglutinative toward each other that practically all the cells became involved and multiple emboli promptly occurred, with the resultant fatal issue. The assumption is that an error in technic was responsible.

Besides the above case a few others have been reported by Ottenberg and Kaliski and others, some of which were fatal while some were not. In a very few, the patients presented warning signs sufficiently early in the course of the transfusion for it to be discontinued. But the accidents resulting from this cause are few and far between. I make it a rule to use only donors whose blood neither hæmolizes nor agglutinates either way with the patient's—whenever possible, even going to the length of having more donors tested out, if they are available and there is enough time, when even slight agglutination is noted. But when additional donors are not available or time is short, I use without hesitation that donor in whose blood there is least to be feared from agglutination, and I must confess that I have never seen the slightest trouble arise either during or after transfusion as a consequence.

The crux of the matter then, as far as agglutination goes, would seem to be that sudden death may be expected or may occur when two bloods are mixed which are actively agglutinative, but in the lesser grades any clumping that may take place simply

amounts to making useless the cells affected, for whenever red cells clump they are necessarily injured and their period of usefulness is over. Therefore, if, for example, one were to introduce 500 c.c. of blood into a circulation and the recipient's plasma should cause agglutination of this blood, little clumps of all the fresh blood would form with the result that the blood might as well not have been introduced, because at one fell blow the cells are all rendered useless—quite aside from the harm they might do the host by plugging up capillaries, or kidney tubules, or by making the host absorb the products of their cell destruction. And if in addition the donor's blood should be agglutinative to the recipient's blood not only would the 500 c.c. introduced be put out of action, but a considerable amount of the host's blood might suffer the same fate; so that instead of helping matters and relieving anæmia, a still further anæmia might be caused. In short, even if no actual disaster does follow agglutination, it is pure waste to transfuse blood where this phenomenon is liable to occur, because the introduced blood is put out of commission immediately, and therefore cannot serve the purpose for which it was intended. Even if only part of it is rendered useless, the waste is considerable and this, taken in conjunction with the danger, is quite sufficient to rule out blood liable to give rise to the phenomenon.

It must be granted, then, that the phenomena of

hæmolysis and agglutination are real dangers in blood transfusion and that every possible effort should be made to eliminate them as complications, for which purpose certain tests have been elaborated whereby their occurrence may be predicted in advance. Unfortunately these tests are rather delicate and require skilled laboratory workers and facilities not found in the ordinary hospital. And, in addition, if they are to be accurate they require not less than one and one-half hours' time (frequently two to two and one-half hours) after blood specimens have been secured from all parties concerned. Certain tests have been suggested which consume less time, but experience has proved them to be correspondingly less accurate than those taking longer to do; so that advantage cannot be taken of tests in the grave emergencies, although I have frequently been able to have them done in certain of these cases by having blood specimens taken the moment transfusion is considered. But it is always hazardous to delay and in one rather recent case of post-operative hemorrhage and shock the wait almost proved disastrous. Decision in the matter simply amounts to determining in which direction lays the greatest risk—letting the patient wait a couple of hours for the result of the tests and run the chance of dying in the meantime, or doing the transfusion and letting the patient take the risk of receiving an incom-

patible blood. To my mind the latter is far the lesser risk of the two because, according to the statistics cited at the beginning of this chapter, out of 800 transfusions, a great number of which were done without preliminary tests, hæmolysis occurred in only about 2 per cent. of the cases. Its true incidence is probably nearer 4 per cent., but even so my feeling is that certain patients will have a much better chance for life by taking this risk than by waiting for the tests to be carried out. And it must always be remembered that even when hæmolysis does occur the majority of the cases recover. Out of six recent emergencies where testing was entirely out of the question, no case of hæmolysis or agglutination occurred, although one patient did suffer a most violent chill about twenty minutes after the transfusion. A certain incompatibility must have been present, but it was not severe enough to cause hæmolysis or affect the course of the patient's illness.[3]

However, in those cases where tests are not to be done or laboratory workers are not available, it is wise to secure as donor the closest absolute blood relative obtainable. The reason for this is that Moss has shown that, as regards hæmolysis and agglutination, all human bloods fall into four permanent, hereditary,

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[3] This was a sodium citrate transfusion and the citrate may have caused the chill. See citrate method of transfusion.

and sharply defined groups and that to a great extent blood relatives come in similar groups. Those bloods which fall in the same group neither hæmolize nor agglutinate each other, so the wisdom of choosing blood relatives as donors in emergencies is apparent. This, of course, is not an absolute rule; I have seen the most violent incompatibilities between brother's and sister's bloods, but so nearly the rule is it that where relatives and non-relatives are tested out, the report frequently comes back that, while one or two of the non-relatives might be perfectly good donors, there is just the faintest suggestion of agglutination between their bloods and the patient's, but no sign of it between the relative's blood and the patient's.

But there is still another factor of safety that gives a certain amount of comfort and security when emergency transfusions become necessary and that is the percentage study that has been worked out for the four groups into which all bloods fall. Approximately it is as follows:

Group I— 2 per cent. of all bloods.
Group II—40 per cent. of all bloods.
Group III—15 per cent. of all bloods.
Group IV—43 per cent. of all bloods.

It will thus be seen that about 83 per cent. of all bloods fall into two groups and the chances are therefore very good that an untested donor and recipient will

fall in one of them. Whether they will or will not, or whether they will be in the same one of the common groups is, of course, purely a matter of chance. But this probably accounts for the comparative freedom from hæmolysis and agglutination encountered in untested transfusions; and it was this unknown state of affairs that gave rise to the early skepticism regarding the occurrence of the phenomena and the necessity for preliminary tests to avoid them. That it is a security upon which too much reliance must not be placed has been amply and repeatedly demonstrated.

The actual tests will be appended.

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CHAPTER VI

SELECTION OF DONOR FOR TRANSFUSION. DANGERS TO DONOR. TREATMENT OF DONOR AFTER TRANSFUSION

The term donor is used to designate the individual who supplies the blood in a transfusion, and the term recipient is used to designate the patient. The recipient is, of course, constant, but the donor is by no means so, except, perhaps, in those few instances where only one person is available as a blood supply and conditions are such that he must be used, suitable or not—fortunately a rare occurrence Human nature is all-enveloping and nearly always volunteers are forthcoming.

It was formerly considered sufficient for the purposes of transfusion to get a big well-built man to act as donor because of the severity of the ordeal he had to undergo and his ability to withstand blood loss with equanimity, but with the advent of definite knowledge concerning hæmolysis and agglutination, there arose the custom of preliminary blood tests which ruled out many apparently good prospective donors. It is still advisable to have a strong young person as donor, but between a well-built, up-standing individual whose blood does not mix with the patient's and an elderly,

anæmic-looking nervous person whose blood does mix there can be no choice—experience has taught the absolute necessity of using bloods of the same group if success is to be attained.

But there are other features besides blood tests to be considered in selecting donors, which may seem trivial to many, but are not at all so to those actually concerned as parties to the transfusion. For instance, the father of a large family might well be passed over in favor of his son or even a volunteer friend, other things such as blood test requirements being equal, in acting as donor to his wife or child. His anxieties are a sufficient burden and personal inconvenience can only make matters worse—and, besides, as bread-winner, his activity might be crippled at a time when it is most needed. For the same reason the sister might at times be chosen instead of the brother.

Age plays but a slight rôle in this question. Naturally the very young and the very old are eliminated, but I have used a boy of seventeen as a donor for his mother, and a man of nearly sixty as donor tc his son, without untoward consequences. One can hardly escape the conviction, though, that if possible only adults between twenty and fifty should be used. Blood loss can hardly be beneficial to a boy or girl still in the growing period, and it is quite conceivable that even temporary weakness due to this cause might be quite harmful to either young or old.

Certain people are eliminated as donors by their temperament, though this was much more common in the days of direct transfusion than it is at present. The anxious parent is not the best donor and a hysterical daughter is hardly to be considered. By the same token, an unwilling donor is an abomination; everything hurts him, he has all sorts of unusual symptoms and I have even had one to actually stop the procedure after giving but a small fraction of the amount desired.

If a direct transfusion is to be done, or even in the case of an indirect transfusion, the nature of the donor's employment deserves consideration as well as the question of his being right- or left-handed. Obviously when a person is right-handed his left arm should be used, if possible, and when left-handed his right arm is preferable and, in the case of two available donors—if one man's work is of a highly skilled, specialized nature, which depends upon his perfect wrist or elbow, and the other man's work is unskilled, the latter should always be chosen.

In certain respects a relative, a near relative, is preferable to a non-relative. The bloods are more liable to be satisfactory, but more important than this is the fact that one feels more justified in taking large quantities from a relative who is usually willing to make a sacrifice, even to the point of several days' inconvenience.

This naturally leads up to the question of paid donors—a latter day development in this work which has been necessitated by a realization upon the part of medical men of the wide therapeutic usefulness of blood, provided it could be obtained in quantities desired without incommoding relatives other than in a financial way. Those in small communities hardly have occasion to consider this matter, since transfusions are of rather infrequent occurrence and donors can always be had from friends or relatives. But in the large cities, the paid donor is playing a decided part in the development of transfusion work. His remuneration is by no means excessive—on the contrary, it is usually small, but, like every other commodity, demand regulates the supply and its cost.

The custom of advertising for men to give up part of their blood for pay originated in New York where it was impossible to obtain suitable donors in sufficient numbers. It must be remembered that the hæmolytic and Wassermann tests eliminate numbers of otherwise good donors, so that it is desirable to test not less than four or five individuals every time a transfusion is in prospect. But advertising for men is not an ideal method of procuring them, and it has been found practicable to obtain them almost at a moment's notice from the various lodging houses frequented by the idle in all large cities. This method

is preferable to advertising—because it makes possible the securing of donors for emergency transfusion, an impossibility, naturally, through the advertising medium. In addition to this, there is the further advantage of familiarity upon the part of the attendants and certain habitués of the lodging house with the procedure of transfusion, thereby rendering it easy to secure men who, under other circumstances, might be timid about sacrificing part of their blood even for large sums of money. As a result of this custom, there has arisen a small group of so-called professional donors—men who have undergone several transfusions and are content to give their blood at rather frequent intervals. I have known men who have submitted to the procedure half a dozen times within two years, apparently unharmed, but since continued blood losses must surely put a strain upon the blood-forming processes of the body which in time might react harmfully upon the individual, I think this custom is not to be encouraged. It is an easy way to make money and I have heard that in New York there are professionals who have given blood more than a dozen times.

With regard to the advisability of utilizing paid donors, I can only say that in my experience they have been more desirable than relatives, because the psychic element of anxiety for the welfare of the patient is totally absent, and, except for a slight timidity for

their own safety (and this is seldom seen), they make brave, even sympathetic, donors. Most of them are young, decent, self-respecting men, temporarily out of employment, who have just enough of the "sporting" element in their make-up to be interested in what is taking place and to be desirous of doing all in their power to bring about a success. It is a common occurrence to have them suggest that no thought be given them in determining the amount of blood to be taken, but I am always extremely careful *not* to take too much, and prefer to take too little rather than incapacitate or weaken a man who depends upon his physical work for his support. In my experience, the amount of blood taken from these donors has always sufficed. When I have thought that I might need more than one man could safely furnish, I have held ready a second one as a reserve supply.

Actual dangers to donors are neither numerous nor serious. I have never lost a donor nor have I ever heard of a person losing his life by giving blood in a transfusion, though I did have one willing, unpaid donor remain in a weakened state of physical relaxation for several months following an emergency transfusion where time to do hæmolytic tests was lacking and the donor's blood, as afterwards was discovered, destroyed the patient's cells in such numbers as to cause the only fatal case of hæmolysis in my series.

The donor was a life-long friend of the recipient and her mental anguish possibly played a part in her failure to recover promptly. She did finally regain her health, and has remained well since.

In the days of direct transfusion, there was more danger to a donor than is the case at present because of the necessity of dissecting out the radial artery and the possibility of infecting the arm through faulty technic. When the recipient was suffering from some communicable disease, such as a pyogenic septicæmia or typhoid infection, the danger was increased, but I, in company with many other surgeons, have been able to carry out a number of such transfusions, without infecting the donor, by means of a technic far more elaborate and painstaking than ordinarily required.

With the introduction of the indirect method of transfusion all danger to the donor has disappeared, except perhaps that of actual blood loss, but since the quantity is rarely over 750 c.c. or 1000 c.c. there is little risk. A certain amount of nausea and occasional vomiting may be seen during the course of blood removal, but if one is careful not to have the flow too fast this can always be avoided. It is wise to direct the donor's attention from the depletion and to distract him by means of conversation and the feeding of bits of cracked ice. I *never* give a preliminary dose of morphine to a donor, though this custom is practised to

a certain extent elsewhere. Morphia tends to lower the blood-pressure and in my experience is entirely unnecessary for reassuring purposes. If signs of nausea appear I try to reassure the donor that he will not be injured in the slightest, and at the same time retard the outflow of blood. If the signs progress, if he turns pale and begins to perspire, the head of the table is lowered a little and he is given some aromatic spirits of ammonia to inhale; if this fails to help and vomiting seems imminent, I immediately stop the operation until he recovers. I have had only one case of this sort in the last three years and in that instance the nausea came so suddenly that it could not be avoided. Sufficient blood had already been taken, so the needle was removed and a prompt recovery ensued.

In some clinics the custom is followed of putting into the donor's vein an amount of salt solution equal to the volume of blood removed, but I have not found this necessary or advisable, since it is my custom never to take more than 800 c.c. of blood from any one, and even this safe amount is taken only from those well able to lose it. The introduction of fluids to make up the deficiency, though, is advisable, and I have a hot cup of cocoa or milk given immediately upon cessation of the operation and then instruct the donor to drink freely of water, tea, coffee, cocoa or milk during the next three or four days. They all follow these instruc-

tions because of the thirst that supervenes upon any appreciable blood loss.

More important than making up the plasma loss is that of retrieving the cellular content of the blood, and to that end I advise rest for a day, not necessarily in bed, plenty of fresh air and nourishing food. I have never given tonics because statistics show that the healthy man or woman will make up the blood lost during a transfusion within four or five days.

If small amounts of blood are removed—250 to 300 c.c.—there is no reason why the same donor should not be used two or three times in succession at intervals of several days; but if larger amounts have been taken it is unwise to use him again under two weeks except in critical circumstances. I have never used the same donor more than three times. Several times, though, I have taken blood from donors who had been used by other operators five and six times; all of them seemed to be in robust health and had not " served " recently; and their familiarity with the procedure made them a great comfort. One of them criticised my technic throughout the whole operation, and, I must admit, to my detriment; but since everything went off according to schedule and he suffered no inconvenience, I think he was reconciled to my shortcomings.

It has often been noticed, but not explained, that in cases where multiple transfusions have been done

on the same patient and different donors have been used, it has appeared that one man's blood was productive of more benefit than another's, although all donors had been carefully tested, were in the same group, and the same amount of blood was used each time with the same technic. In one of my cases where six transfusions were carried out, this fact was so striking that I used the first donor a second time and demonstrated the greater efficiency of his blood as compared to that of the others. Whether this is due to the donor's blood or to different phases of the patient's condition is not clear, but it is a feature worth keeping in mind whenever multiple transfusions are in order. Perhaps later serological studies will shed more light on the phenomenon.

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CHAPTER VII

METHODS OF TRANSFUSION. TECHNIC

The transfusion of blood may be accomplished either by having the blood flow from the vessels of one individual directly into the vessels of another, this procedure being known as *direct transfusion,* or the blood may be removed from one person and injected or allowed to flow into the vessels of another, this procedure being known as *indirect transfusion.*

The direct method was first to become popular because of Crile's epoch-making work on blood transfusion some ten or twelve years ago. He perfected a little silver tube and evolved a suitable technic whereby an artery of one person could be united with a vein of another with such accuracy that blood would flow without hindrance directly from one to the other and for as long a time as was necessary or desirable. This was the real beginning of transfusion as we now know it. Hitherto, it had been practically impossible to transfer blood with any degree of accuracy or certainty by any of the methods extant, so that when Crile's tube and technic made their appearance a long-felt need was fulfilled and it was not long before reports of transfusions began to appear with increasing frequency.

Thus it came about that many workers centred their attention on this fascinating subject, with the result that it soon became apparent that Crile's tube had many decided limitations, chief among which was the not inconsiderable amount of special training required before one could really use it with uniform success. Many modifications of the tube were suggested, all with the view to simplification, and several decided improvements were suggested, but further work demonstrated the fact that a tube of an entirely different constructive principle would answer the purpose just as well and require far less special training for its employment. Crile's tube gradually fell into disuse and the newer instruments took its place, all, however, being adapted only for direct transfusion. But there were always two serious drawbacks to the direct method—the amount of blood transfused could not be accurately measured and an incision in both donor and recipient was required each time it was done, the radial artery of the donor being sacrificed in every instance. Serious as these difficulties were, the need for a change did not become really urgent until the field for transfusion began to widen to such extent that its usefulness seemed likely to be greatly curtailed unless the blood amount could be accurately measured and donors could be used without being subjected to an operation, with its consequent disability. Then it was that indirect trans-

fusion, which had been tried and discarded years ago, again made its appearance in the form known best as the needle and syringe method of Lindeman, whereby blood was withdrawn by means of a needle inserted into the donor's vein, and injected in a similar manner into a vein of the recipient, successive syringes being employed. This method was cumbersome and presented other deficiencies, but the need for it was great and its use slowly and surely spread. Later on modifications made their appearance and from it have developed several methods whereby blood can be indirectly transfused with far greater ease, rapidity and accuracy than ever before, as a consequence of which the death knell of direct transfusion has been sounded. Occasions will undoubtedly present themselves when the direct method should be used—but these will become constantly rarer.

From the foregoing sketch, one might conclude that the last word in transfusion methods has been said—and so it has, perhaps, so far as the whole, untreated blood is concerned, but it is by no means certain that the future will deal with blood in its natural state. The difficulty is that blood clots with great rapidity, which makes it difficult to work with, and limits its possible usefulness, so that there has come about the need for some means of preventing coagulation or at least delaying it. To this end anticoagulants, long known and made use of for experimental purposes,

have assumed practical clinical importance. It is unnecessary here to detail the work on the substance known as hirudin further than to note its failure as far as humans are concerned. More to the point is the consideration of *sodium citrate* which in the hands of Lewisohn of New York has given practical results of most promising character. By using this drug in a dilution of two-tenths of one per cent. (0.2 per cent.) Lewisohn demonstrated that blood could be kept uncoagulated for hours, over forty-eight hours, and at any time during that period it was suitable for transfusion.[1] Other workers have confirmed Lewisohn's results and the method, while still in the probationary period, is constantly making new friends. That it will eventually supercede all other methods, perhaps in a modified form, I have no doubt.

Thus we really have three methods of blood transfusion, *the direct, the indirect whole blood* and the *indirect anticoagulation* method and, since there are several ways of accomplishing each, I will give in detail several of the best methods under each heading.

DIRECT TRANSFUSION

Crile's Method

"The vessels to be anastomosed (radial artery of donor and an arm vein of the recipient) are exposed,

[1] Personally, I feel that it is unwise to use blood that has been out of the body longer than twelve hours.

and, after selection of a cannula (Fig. 1) of size suitable to the size of the vessel, the end of the vein is pulled through the handle end of the tube by means of a single fine suture inserted in its edge (Fig. 2), the needle being left on the suture and passed through the cannula ahead of the vein. The handle of the cannula is then tightly seized by a pair of hæmostats, three mosquito hæmostats are snapped at equidistant points on the end of the vein, taking care not to have

Fig. 1.—Crile cannula.

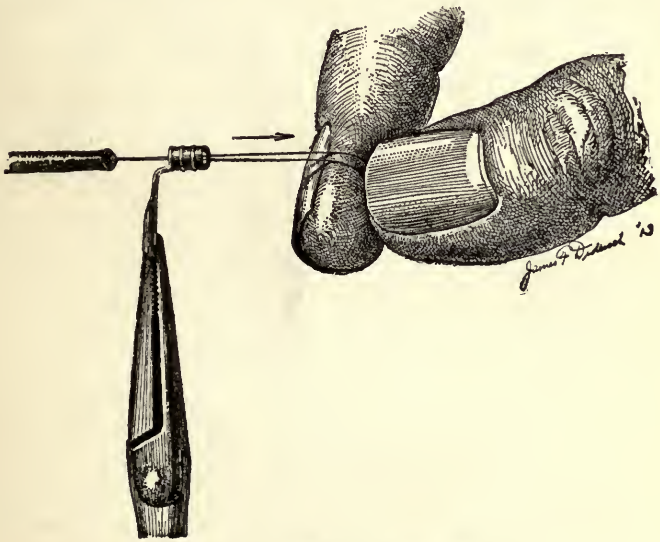

Fig. 2.—Drawing vein through cannula.

the tips extend up into the lumen more than is necessary to get a firm hold. The end of the vein is then cuffed back over the cannula by gentle simultaneous

traction on the three hæmostats (Fig. 3) and tied firmly in place with a fine linen thread in the groove nearest the handle (Fig. 4). The cuffed part is next covered with sterile vaseline, being careful not to get any into the open end. This facilitates slipping the

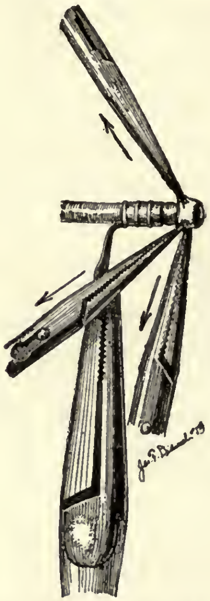

FIG. 3.—Cuffing vein back over the cannula.

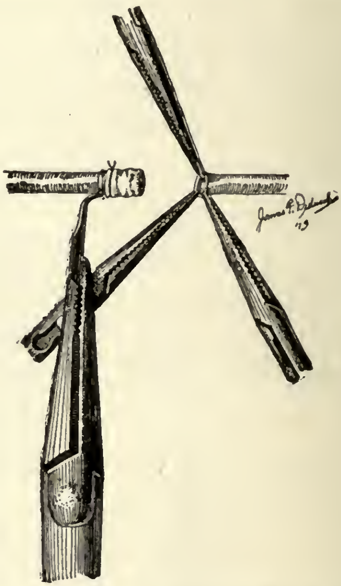

FIG. 4.—Vein cuffed and tied in groove nearest handle of the cannula. Artery grasped by three mosquito clamps.

artery over the cuff. The hæmostats are removed from the full edge and the artery may then be put in place.

"Owing to the elasticity of the arterial wall, it usually shrinks (contracts) considerably when the pressure from within is removed, as it is at the free

end. To obviate this it may be necessary to dilate the end very gently by inserting the closed jaws of a mosquito clamp covered with vaseline and opening them for a short distance. The three hæmostats are applied to the edges, just as with the vein, and the artery is gently drawn over the cuffed vein on the cannula and tied in place with another fine linen suture applied in the remaining groove (Fig. 5). The mosquito hæmostats are removed. The process is then completed. After the transfusion the cannula is removed, both artery and vein are ligated and the wounds are sutured.

FIG. 5.—Artery slipped over cannula and tied in the second groove. Anastomosis complete.

"In making a cannula anastomosis, experience will show what size cannula is suitable for given vessels. As large a size should be used as possible, without injuring the intima of the artery by stretching it too much. Usually there will be no difficulty in obtaining a large vein, but the artery may be very small. If too small a cannula is used the volume of the flow will be diminished. Moreover, too large a vein will take up too much room in the cannula and the amount of the flow will be diminished.

"The exposed vessels should be kept moist and warm with normal salt solution. Not only is drying harmful, but the flow is increased through gradual relaxation of the arterial wall.

"Experience has shown that if anything goes wrong in carrying out this technic, it is best to start again from the beginning, and not to try to get around any of the details by substitution."

Elsberg's Method

The second cannula is an ingenious device of Elsberg. It is built on the principle of a monkey-wrench (Fig. 6) which can be enlarged or narrowed to any size desired by means of a screw at its end. The smallest lumen obtainable is about equal to that of the

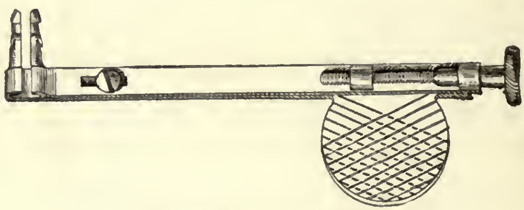

Fig. 6.—Elsberg's monkey-wrench cannula.

smallest Crile cannula, and the largest greater than the lumen of any radial artery. The instrument is cone-shaped at its tip, a short distance from which is a ridge with four small pin points which are directed backward. The lumen of the cannula at its base is larger than at the tip. The construction of the cannula can be easily understood from the following description of the method of using it:

"The radial artery of the donor is exposed and isolated in the usual manner. The cannula, screwed

wide open, is then slipped under and around the vessel. It is then screwed shut until the two halves of the instrument slightly compress the vessel (Fig. 7). The artery is then tied off about one centimetre from the tip of the cannula. Before the vessel is divided, the three small-eye tenacula are passed through the wall of the artery, at three points of its circumference, a few millimetres from the ligature. Small mosquito forceps may also be used. These

Fig. 7.

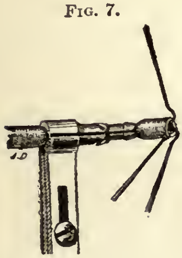

Fig. 8.

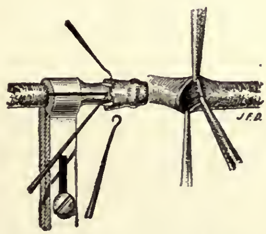

Fig. 9.

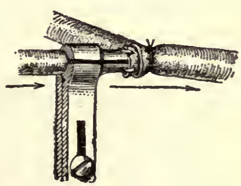

Fig. 7.—Artery "set" in Elsberg's cannula; tenacula in position for cuffing.
Fig. 8.—Artery everted and impaled on the hooks. Vein grasped by mosquito clamps.
Fig. 9.—Cannula slipped into side of vein and tied in position. Anastomosis complete.

are given to an assistant, who makes traction on them while the operator cuts the vessel near the ligature. The moment the artery is cut, the stump is pulled back over the cannula by means of the tenacula or forceps, and is held in place without ligation by the small pin-points (Fig. 8). There is no bleeding from the artery, even though no hæmostatic clamp has been applied, because the cannula itself acts as a hæmostatic clamp. The vein of the recipient is then

exposed (but not freed), two ligatures are passed around it, one is tied peripherally in the usual manner. A small transverse slit is made in the vein, the cannula with the cuffed artery inserted into the vein, a ligature tied around the vein and cannula screwed open (Fig. 9) and the blood allowed to flow. The rapidity of the flow can be varied as desired by the size to which the instrument is screwed or unscrewed, and the lumen of the artery is never diminished.

" It will be noticed that the artery is cuffed instead of the vein; this method I believe to be more correct. The vein is the larger vessel and can therefore be more easily telescoped over the artery. The vein is only exposed, not freed, and the artery is intubated into it.

" With this cannula I have been able to make the anastomosis in less than four minutes after the artery had been isolated, and have found the entire procedure a simple one. The advantages of the instrument are the following:

"(1) One cannula will fit any vessel.

"(2) The cannula is applied around the vessel instead of the vessel being drawn through the cannula.

"(3) No ligature of the cuffed vessel is required.

"(4) The cannula itself acts as a hæmostatic clamp.

"(5) The cuffing of the artery is easily accomplished without stripping back the adventitia, and,

therefore, the traumatism to the artery wall is reduced to a minimum.

"(6) The vein need only be exposed, not dissected out and cut.

"(7) As the cannula is unscrewed the blood will flow, the flow can be regulated at will, and the lumen of the artery is not diminished."

Bernheim's Method

The third instrument which I shall present is one of my own design. Simple in construction, large enough to work with comfortably, it requires a mini-

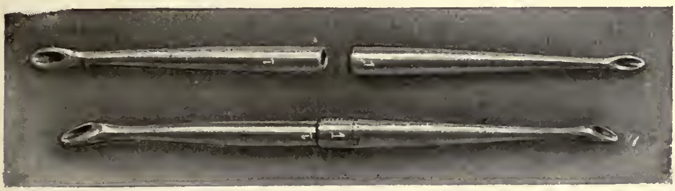

Fig. 10.—Author's two-pieced transfusion tube.

mum of dissection and can be rapidly put into action. It is a two-pieced affair (Fig. 10) consisting of two hollow tubes, each 4 cm. long, and each bulbous at one end in order to form a neck for a retaining tie or specially devised clamp, and bevelled to facilitate entrance into the vessel; the other ends are tubular and fitted for invagination. The instrument was originally constructed in two sizes as regards the bore of the smaller ends, but experience has shown that either

size will fit the vessels of any individual—from an infant up to an adult.

My reason for having an instrument thus constructed in two separate parts was twofold. First, in transfusing an infant, it is usually difficult to make the actual union of vessels with a small instrument like that of Crile or Elsberg because of the smallness of the parts and the delicacy of the infant's vessels. Paraffined glass tubes answer the purpose fairly well, but paraffin is not always at hand, nor is a suitable glass tube, and, if it is, the probabilities are that it will be chipped or broken. Second, for emergency work, I believe that a cannula constructed in two pieces, one of which can be rapidly inserted into the artery of the donor, and the other into the vein of the recipient, by separate screws of operators, is best. Even in cases where haste has not been so urgent, the ordeal for the recipient, who is usually anxious and in a precarious state, can be materially relieved by preparing the donor completely before bringing the recipient into the operating room, or even by preparing the two entirely in separate rooms, simply wheeling the stretcher of the donor into the recipient's room, placing them in apposition, and invaginating the two halves of the cannula—a matter of only a few seconds.

The technic, then, of a transfusion by means of this two-pieced cannula, as well as the management

of direct transfusion in general, is as follows: The radial artery of the donor is usually united to one of the superficial veins at the elbow of the recipient; occasionally because of infection at the elbow, it becomes necessary to employ a vein of the leg, generally the internal saphenous, although any available vein may be used. But no matter whether it be arm to arm, or arm to leg, in preparing the patient the watchword should be "left to left, right to right"—in other words, the left radial should always be united to a vein of the left arm or leg and *vice versa;* a few moments' thought will show the anatomical reasons for this. Other things being equal, it is always wise to leave the choice of radials to the donor, but where he (or she) has no choice, it is my rule to utilize the left radial, if the patient be right-handed and both radials are of the same size (which, by the way, is not always the case), his right if he be left-handed. Thus the donor will be incapacitated as little as possible during the healing of his wound—a detail, perhaps, but one that ought to be considered.

Time will be saved if the radial is dissected out as follows, novocaine (0.5 per cent.) being the anæsthetic of choice: (1) Expose the artery with its accompanying veins for a distance of about two inches; (2) free the artery from the veins and tie off all branches doubly with very fine silk, cutting between

the ties; (3) tie off the artery doubly at the distal end of the wound and cut between the ties, thus allowing about one and one-half inches of the vessel to lie free in the wound; (4) tie off all bleeding points in the wound, and keep a constant stream of warm salt solution flowing over the artery, all sponging being done with gauze moistened in the same solution; (5) place a bull-dog clamp on the vessel at the proximal end of the wound.

Up to this point the technic is the same no matter which method of anastomosis is to be used. If my two-pieced cannula is to be employed, a small cut is now made in the upper side of the artery with a fine pair of scissors or a knife, the opening being made at right angles to the course of the vessel and about half its width. Next, every visible trace of blood is immediately washed out with warm salt solution and liquid vaseline, the latter being injected into the lumen of the vessel with a medicine dropper at frequent intervals during the washing process. It keeps the vessel soft and pliable, and prevents too rapid evaporation and consequent drying. Any little bit of adventitia that may get into the opening should be carefully pushed away or cut off.

The vessel having been carefully prepared, the bevelled end of the male half of the tube is inserted in the artery and held there by a tie thrown around its

neck (Fig. 11).[2] Liquid vaseline is now again injected into the vessel through the tube, and the whole thing wrapped in salt solution gauze to await the completion of a similar preparation of the vein of the recipient. It is hardly necessary to dissect out more than one inch of the vein, and, as this is always quite superficial, the time required for the whole procedure of dissection, cleansing, and insertion of the female half of the tube amounts to hardly more than five minutes.

When both patients have been prepared, their stretchers are brought into apposition and the two arms are placed on a table about one foot broad. With a little manipulation the wrist of the donor is brought into such proximity to the elbow of the recipient that the tubes can be invaginated to the proper degree (Fig. 12). When this is accomplished, a steady stream of warm salt solution is started flowing over the artery, tubes, vein, and the bull-dog clamp is removed from the vein, its place being taken by the thumb and the first finger of the right hand of the operator. With great care the clamp controlling the arterial flow is now gradually released, coincidently with which the thumb and finger controlling the vein gradually ease up, thus permitting the blood to go

[2] A special clamp has been devised for this purpose, thus obviating the necessity of using a single tie during the course of the transfusion—except for closing purposes.

FIG. 11.—Bernheim's Transfusion of Blood.

Fig. 12.—Tubes invaginated and anastomosis complete.

over gradually, so as to prevent any possibility of swamping, or embarrassing the circulation of the recipient by a sudden gush of blood under great pressure. Let it be strongly emphasized here that, with few exceptions, the margin of safety is none too great in any transfusion at any stage. It is wise, therefore, to control the inflow in the manner above described during the entire course of the transfusion.

If assistants are at hand, the blood-pressure and pulse of the recipient should be taken at intervals of every three minutes, that of the donor every five minutes. These measures cause but slight annoyance to the patients and are of the utmost importance to the surgeon in judging the condition of both individuals. Hæmoglobin and red counts, made during the course of the operation, although they are interesting and valuable, do not give nearly so helpful immediate information as do blood-pressure and pulse, and, since they cause more or less discomfort to the patients, we do not make these readings unless there is some special reason for them. It is unnecessary to say, of course, that the blood-pressure and pulse of both donor and recipient have been taken before starting the transfusion, as a control, and that if the facilities are at hand, a complete blood examination—reds, white, and hæmoglobin—has been made of both patients, also as a control, for after completion of the transfusion these

data are most valuable in interpreting both the immediate and future results of the operation.

Where the recipient is practically exsanguinated, and there is no contra-indication, it is wise to give him all the blood he can conveniently hold, even occasionally (Crile) going to the extent of using two donors in case one cannot stand any great loss of blood. My routine is to attempt to bring a pulse of say 150 or 160 down to about 100 and to raise a blood-pressure of 50 to 70 up to 110 or 120, figures well within the zone of safety.

It sometimes happens that it is decidedly unwise, even hazardous, to overload the circulation, an example of such a case being a patient exsanguinated as a result of hemorrhage from typhoid (or other) ulcers of the bowel. To give such an individual much blood would be tempting fate, whereas a small amount, sent in slowly, will decrease the coagulation time, and seal up the mouths of open vessels with life-saving thrombi. In other words, a great amount of blood will simply raise the blood-pressure to such an extent that it will literally blow out any soft young plugs that might be all that is holding body and soul together.

It is a most difficult matter to judge as to the exact amount of blood that has gone, or is going over. No practical method of measuring the amount of blood flow in a direct transfusion has been devised, and

until this much-desired instrument is placed at our disposal we shall be compelled to depend upon clinical signs for an index of the amount of blood transfused. It must be recognized that a number of factors must of necessity enter into any calculation of bulk. The blood-pressure, because of the psychic disturbance in every operation of this sort, is by no means constant. The loss of blood is another, perhaps the chief, factor in determining the instability of the blood-pressure and therefore the amount that goes over in bulk. The pulse-rate varies, too, from time to time and this must be considered in any determination of amount. There are still other factors, such as the viscosity of blood, etc., which need not be considered in a work of this character. It is sufficient to say that to the careful, experienced surgeon all the factors above mentioned can be determined with a surprising degree of accuracy by the thumb and forefinger guarding the entrance to the vein. This knowledge and constant observation of the actual blood-pressure reported by the assistants, the general appearance of the patients, and the actual time that the blood has been flowing—all these serve as a guide to the amount of blood going over, and the proper time to cease transfusing.

In regard to the duration of actual flow in transfusion in general, there are various questions to be considered. An infant will require but a small amount

of blood (children need far less than adults), and, as a rule, women less than men, always considering that the patient is exsanguinated. A big strong man will generally have a larger radial than a small man, and his pressure will enable a much larger and more powerful stream to be thrown by his vessel. Likewise, a female donor may give less blood in a given time than a man—provided the man is not too badly frightened. Thus, the actual time of transfusion varies from three to five minutes to one hour or even an hour and a quarter if a very small cannula is used or if the blood has been permitted to go over very slowly. For most transfusions the average duration of the flow is from twenty to forty minutes.

The welfare of the donor in transfusion must be carefully watched. I have transfused from one donor for over an hour without any signs of distress, while in another case fifteen minutes were sufficient to produce great anxiety. In general a sudden fall of twenty to thirty points in blood-pressure should warn the operator that the limit has about been reached. Unfortunately, however, a blood-pressure apparatus is not always at hand and even when it is, the fall in pressure, sudden or gradual, does not always occur. In such instances any sudden pallor, accompanied by nausea and vomiting, continued and increasing thirst, great restlessness, together with a decrease in blood-

pressure as shown by the finger of the operator on the donor's radial, may serve as the needed danger signal. The bleeding should never be permitted to exceed the limit of safety; the donor ought never be allowed to collapse utterly. A proper appreciation of his own responsibility as well as the moral rights of those courageous individuals, generous enough to give of their own blood that another might live, should always be pre-eminent in the mind of the surgeon who undertakes work of this nature.

INDIRECT TRANSFUSION

Coming to the indirect methods, one has again the opportunity of choice, and various factors influence one in a determination of method, such, for instance, as the number of assistants at hand, the ability to move the patient or the desirability of doing so, *et cetera.* It may be said in general that intimate familiarity with one single method is greatly to be desired, although a working knowledge of several is conducive to the best results, flexibility in matters of this sort being always of advantage.

The first indirect method of transfusing blood that was of any real practical worth was devised and perfected by Dr. Edward Lindeman of New York and for a time it was the only indirect method in use. But it has serious drawbacks in that three assistants

are essential to its proper use and unless the " team " works together with rapidity and precision, certain accidents may take place of such character that the blood transfer is delayed, or interfered with, or even prevented. So that modifications of Lindeman's method presently appeared, one of which was devised by Unger, also of New York, another by myself, and still others by a number of different men, the cardinal principle of all being about the same though differing somewhat in construction and execution.

Proceeding along somewhat different lines, Kimpton and Brown of Boston devised an indirect method of collecting blood in a paraffined glass cylinder and then injecting it, while a somewhat similar apparatus was devised by Satterlee and Hooker.

The latest method—and the one that really holds out more promise of permanent usefulness than any other—is that known as the citrate method as conceived and perfected by Lewisohn of New York and almost coincidentally by Agote of Argentina.

Sodium citrate is an anticoagulant long known to laboratory workers, and used by them experimentally, but always considered too toxic for human use, so that when Lewisohn suggested that it could be used with perfect safety in 0.2 per cent. strength solution, a great deal of skepticism was expressed even in the face of his carefully planned animal experiments and his

successful clinical demonstrations. This lack of enthusiasm was unfortunately strengthened by a few early unsatisfactory reports by scattered clinicians whose work did not bear close inspection. Several deaths were chronicled and numerous sequelæ were attributed to the use of citrated blood that have been found by more competent observers to have been the result of errors in hæmolytic tests, and in the carrying out of the actual transfusion technic, rather than to the use of citrate. This unsettled state of affairs, though, has resulted in delaying the widespread use of the method and has to a certain extent cast a shadow over its many merits. For there can be no question but that a great step forward was taken when it became possible to take uncoagulable blood to a patient's room and in a leisurely manner have it pass into his veins without in the least disturbing him other than by possibly dissecting out a small segment of his vessel—though even this is unnecessary in those cases where a vein of sufficient calibre to accommodate a needle can be seen or felt. By some this is felt to be a matter of small importance, but such a view can only be held by the inexperienced. Those who have actually witnessed exitus of the desperately ill as a result of or during the comparative slight manipulations necessary to a transfer from bed to stretcher or even from moving the bed on to or off of an elevator

know better. Even where actual demise does not follow, it is a well known fact that simple transfer of patients from the ward or room to the operating room lowers their overtaxed vitality. I cannot lay too much stress on this point.

Nor is this the only claim for recognition of the citrate method, since by this method transfusions in the home will be greatly facilitated and at no time will it be necessary for patient to see donor or *vice versa.* I do not mean to advocate transfusion in the home—on the contrary, it is to be avoided—but every once in a while cases of the utmost urgency arise where it becomes necessary to carry out a transfusion in the home, a rather difficult and tiresome procedure, until now. The separation of donor from recipient eliminates at one fell blow the depressing psychical element from blood transfusion, a most fortunate event, especially in cases where near and dear relatives act in these capacities. The Kimpton-Brown method of transfusion some time ago eliminated this feature to a degree but it has certain drawbacks common to all methods where whole untreated blood is used that are not to be found in the citrate method.

I have used many different instruments for transfusion, several of which I devised, and I have passed through the successive stages of fearfully difficult and trying direct transfusion with Crile's tube and my

little three-pronged modification, to the direct transfusion with longer glass and metal tubes. And from that stage, along with the other workers, I passed to the period of indirect transfusion by Lindeman's needle and syringe, which for a time seemed to satisfy —but only for a time, because of its clumsiness. Modifications of this method then made their appearance in the form of tubes containing a central revolving plug, one of which I devised and used many, many times with the utmost success and satisfaction—as did many others. But I am frank to admit that no method and no instrument is comparable in facility and elasticity to the citrate method of transfusion and I feel that a debt of gratitude is owing to Drs. Lewisohn, Weil, and Agote for working out its details so carefully. Of late I have used this method in preference to all others and venture to predict that within a few years all our cunningly devised instruments for transfusion will be of interest merely as curiosities. They have served their purpose admirably but their day is waning.

My reason for giving a few of the indirect methods of transfusion is that they are still in use to a great extent and will probably continue to be employed, although in decreasing proportion as the citrate method becomes more familiar.

LINDEMAN'S METHOD

" The entire apparatus for simple syringe transfusion consists of two sets of cannulas, two tourniquets and twelve syringes.

CANNULAS

" Two sets of cannulas are employed, one for the donor, the other for the recipient.

There are three cannulas to each set (Fig. 13, 1, 2, 3). Each cannula telescopes within the other as shown in Fig. 14.

The innermost cannula is practically a hollow

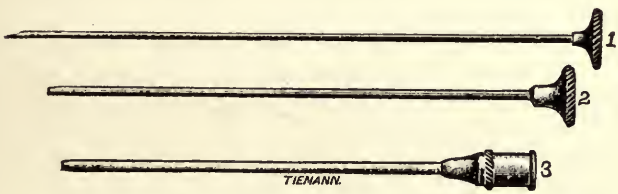

FIG. 13.

needle, 2 6/16 inches long, 20-gauge, with one end ground to a fine point and short bevel. The hollow needle (1, Fig. 14) is fitted snugly into cannula 2. Cannula 2 is 5 mm. shorter than the needle and is

FIG. 14.

fitted snugly into cannula 3. Cannula 3 is 5 mm.

shorter than cannula 2. The proximal ends of 1 and 2 are capped with stationary thumb-screw caps.

The proximal end of 3 is capped with a receiver to fit any Record syringe.

Cannula 3 is 2 inches long, 14-gauge, .064 diameter. The calibre of this cannula is the same as the tip of a Record syringe.

In very small infants with very small veins only cannulas 1 and 2 are employed, 2 being capped with the receiver to fit tip of syringe.

The syringes used are Record syringes of new improved type with a capacity of 20 c.c. and can be sterilized by boiling.

OPERATION

" One operator manages syringe of recipient. Another operator manages syringe of donor. An assistant stands between operators, who are in a position close to the assistant. Donor and recipient are placed in the recumbent posture. Suitable veins are selected.

In adults and most children over two years of age the median basilic is easily accessible. In infants the external jugular or one of its tributaries is entered more advantageously. In some cases the internal saphenous may prove the vein of preference.

A tourniquet is placed in position, and the skin is sterilized with iodine. The cannula is then held in a position almost parallel to the vein with the thumb

on the thumb-screw cap of the innermost cannula (1, Fig. 14). The skin is then punctured and the cannula is forced into the vein. After the first joint A has entered vein, Cannula I is withdrawn a distance of about one-half inch. (This prevents the vessel wall from being injured or punctured by the needle after the vein is entered.)

With the thumb now on the thumb-screw cap of 2 the cannula is forced in until the second joint B (Fig. 14) has entered the vein. Cannula 2 is then withdrawn a distance of about one-half inch (cannula 3 alone can come into contact with the vessel wall). Cannula 3 is then gently pushed into the vein to a desirable length; usually three-quarters to one inch will suffice.

Cannulas 1 and 2 are now withdrawn entirely. If the vein has been successfully entered, blood will flow through the cannula. When the first drop appears a syringe containing warm saline solution is immediately attached and a very slow flow of saline is maintained through cannula. Escape of blood is thus prevented.

There is no need of haste at this stage.

A cannula is next inserted in vein of donor in a like manner; again a syringe containing warm saline is attached and loss of blood thus prevented. Everything is now in readiness for the transfusion. An

empty syringe is substituted for the one containing saline solution, and blood is withdrawn from donor as rapidly as possible. When the syringe is full the assistant passes it to the operator on the recipient, who removes its saline syringe, attaches the syringe containing blood and evacuates the contents gently but speedily into the vein.

One syringeful of blood is followed by another in rapid succession until the desired quantity of blood has been transfused.

A little normal saline is injected through cannula of recipient after each syringeful of blood. This keeps cannula free of blood and precludes the possibility of clotting.

It has been found advisable for the assistant (or third man) to remove the syringe from the cannula of the donor as soon as filled. The operator can thus hold the cannula in place with one hand while with the other hand he may at once adjust an empty syringe into the cannula. Loss of blood is thus reduced to a minimum.

RULES

"1. Bright polished surfaces of syringe and cannulas are requisite.

2. A syringe used once should not again be employed until thoroughly cleansed with sterile water.

3. Air must be avoided. This, however, offers no difficulty.

4. Tourniquet of patient must be removed after vein is entered with cannula.

5. Tourniquet remains on donor throughout operation; momentary release of tourniquet may be advisable once or twice during course.

6. Dexterity and speed are requisite for success.

7. Syringes can be evacuated more rapidly than they can be filled without any harmful effects. This difference in time allows for attachment of syringe with warm saline following each syringeful of blood.

COMMENTS

" The time elapsing in filling and evacuating the syringe is so brief that blood does not undergo any alteration from donor to recipient.

No lubricant has been employed except in one case. Cannulas are lined with a film coating of albolene.

Both arms of the donor may be used simultaneously.

Larger syringes with larger calibred cannulas may be used, but the present sizes have worked satisfactorily and fittings of syringe and cannulas are of universal gauge.

Syringes and cannulas may be kept sterile in individual metal containers. They are thus in readiness

for immediate use and no preparation for operation is required.

The same vein can be used repeatedly for subsequent transfusions, since no thrombosis nor permanent injury to vessel occurs.

Any quantity of blood can be transfused and the quantity is definitely measured at the time of transfusion."

UNGER'S METHOD.

"The instrument (Fig. 15) I have devised eliminates the causes of the difficulties experienced in the syringe-cannula method. Fundamentally, it is a stopcock, which alternately connects a syringe for blood to the donor and at the same time a syringe with saline to the recipient; then by turning the cock the syringe with blood is immediately connected to the recipient and the syringe with saline to the donor.

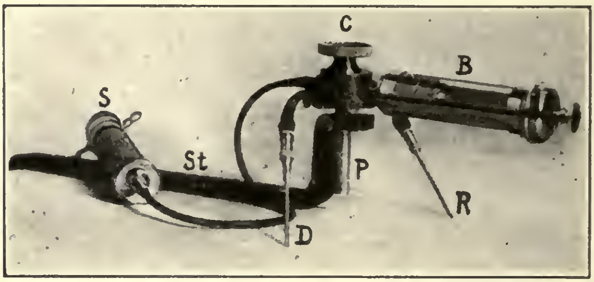

FIG. 15.—Unger's instrument for indirect transfusion. (*J. A. M. A.*, February 13, 1915, vol. lxiv, No. 7.)

THE INSTRUMENT

" A cock which has four outlets constitutes the central part of the instrument. The outlets are designated as follows: (1) Blood outlet (B); (2) saline outlet (S); (3) recipient's outlet (R); (4) donor's outlet (D).

(1) Blood outlet (B): To this is directly attached a 20 c.c. "Reformed Record" syringe (Syr.). Through this outlet, by means of the syringe, the blood is aspirated or injected.

(2) Saline outlet (S): To this is attached a long piece of rubber tubing, the other end of which has connected to it a syringe for saline. The exact length of the tube is immaterial. It should, however, be long enough to get the assistant who is attending to the injection of saline out of the way of the operator. The material of which the tube is made is likewise unimportant, since nothing but saline passes through it. Instead of a plain syringe, a slightly modified Wechselmann salvarsan apparatus may be used. The latter, by means of two ball-valves, allows of the ready filling and emptying of the syringe, and eliminates the necessity of disconnecting it.

(3) and (4) Recipient's and donor's outlet (R and D): To each of these is connected a paraffined rubber tube 1¾ inches long, which has attached to its other end a metal connecting piece. This, in turn, fits

the recipient's and donor's cannula. The tubing is a piece of catheter (No. 15 French) which is paraffined according to the method described by Dr. G. E. Brewer. They are sterilized, and then for a few seconds immersed in boiling paraffin. The tube is then shaken in the air in order to distribute the paraffin equally, to get rid of the excess, and to hasten hardening.

The cock is so arranged that the central stopper (CS) can be rotated only through an arc of 45 degrees. This range of rotation allows of three possible positions, in two of which two simultaneous circuits exist; in the third no circuit whatever is present. Naming the positions according to the flow of blood and the circuits according to the outlets they connect, we have:

1. Donor's position, establishing (*a*) donor blood circuit and (*b*) recipient saline circuit.

2. Recipient's position, establishing (*a*) recipient blood circuit and (*b*) donor saline circuit.

3. Intermediate position, establishing no circuit—all outlets are shut off.

1. Donor's position: If the cock be turned toward the donor as far as it will go, the instrument will be in the donor's position. A channel (donor blood circuit) between the donor's vein and the Record syringe is established for the aspiration of blood. At the same

time, another channel (recipient saline circuit) exists, through which saline is injected into the recipient's cannula in order to insure its patency.

2. Recipient's position: If the cock be turned toward the recipient as far as it will go, the instrument will be in the recipient's position. Here again, two channels exist, one through which the blood is injected into the recipient (recipient blood circuit), and one (donor saline circuit) which connects the donor with the saline syringe so that this circuit can be kept patent. It is this immediate and continued flushing with saline of that part of the system through which blood is not passing that insures freedom from clotting.

3. Intermediate position: If the cock be turned midway between the donor's and the recipient's positions, the instrument is in the intermediate position, and all the outlets are closed off.

The instrument is supported by a stand, which is merely a mechanical device to hold the cock stationary and to permit of its adjustment to various heights in conformity with the levels of the veins.

TECHNIC

"After having firmly fixed the stand to the table, the cock, with the tubing attached to the donor's and recipient's outlets, is fastened to the stand. The saline apparatus, from which all air has been forced out, is

connected to the saline outlet. The cock is put in the donor's position and here also the air is forced out by means of saline. By raising, lowering, or rotating the pedestal, to which the instrument is attached, and by proper placing of the arms, connections to the cannulas can be made without difficulty.

Into the recipient's vein is inserted a large cannula, which is then connected to the recipient's outlet. Since the cock is in the donor's position, saline can be slowly injected into the recipient, thereby insuring the patency of this cannula. Into the donor's vein is inserted a cannula which is now attached to the donor's outlet. It is important to insert the cannula so that it points toward the donor's hand rather than the tourniquet. Blood immediately runs out of the blood outlet, forcing the air ahead of it. Into this outlet, a Record syringe is placed and blood aspirated. When the syringe is filled, the cock is turned into the recipient position and the blood injected. Since the assistant is always very slowly injecting saline, he is now flushing the circuit which was used in getting the blood into the syringe. As soon as the 20 c.c. of blood have been injected, the cock is turned back to the donor's position, and the syringe refilled. This is continued until the desired amount of blood has been transfused. The syringe need not be changed after each injection, but may be refilled until it begins to work with difficulty.

Before the syringe is disconnected, the cock should be turned to the intermediate position so that there is no loss of blood.

After connections have been made to the cannulas: (1) The operator (*a*) aspirates and injects blood, (*b*) changes the syringe when necessary and (*c*) turns the cock back and forth. (2) The assistant merely slowly forces saline out of his syringe. (3) The nurse cleans the Record syringes as fast as they are used and places a clean one in easy reach of the operator.

ADVANTAGES OF THIS METHOD

" The instrument I have described overcomes the difficulties experienced with the syringe-cannula method, by striking at their causes.

1. The frequent handling of the cannulas is eliminated because the connections are made not directly to them but to the cock. For this reason the cannulas ought not to be dislodged.

2. Clotting is avoided because the entire system is regularly and instantly flushed with saline, and the length of time the blood is outside of the body is reduced to a minimum. In none of the animal experiments did clotting occur.

3. Only the operator handles the blood syringe. The function of the assistant is limited to the injection of saline.

4. Fewer syringes are needed. In one experiment, 800 c.c. of blood were transfused, only two syringes being used. It is advisable, however, to have about four to meet emergencies.

5. It is time-saving because it reduces the manipulations; it minimizes the time the blood is outside of the body, and it allows of the injection of saline simultaneously with the aspiration or injection of blood. When indicated, a more rapid transfusion can be done by this than by any other method. The rate of flow can, however, be varied at will. Blood can be sent across as slowly as one wishes, because the patency of the circuits can be relied on."

Bernheim's Method

" Briefly, the apparatus consists of two needles, one of which is inserted into a vein of the donor, the other into a vein of the recipient, and a U-shaped tube, at the midpoint of which is a pocket into which a hollow revolving plug is fitted (Fig. 16). This plug is open at one end so as to accommodate the nozzle of a Record syringe (the plug may be made to fit any other form of syringe desired), but is closed at its other end, the point of exit being in one side so as to correspond to the openings of the two arms of the U into the central pocket. The distal ends of the arms, then, are attached to six inches (or more) of rubber tubing each of which is in turn attached to the needles which

have been placed in the donor's and the recipient's vessels.[3] A circuit having been completed in this manner, blood is withdrawn by means of a syringe from the donor, and the plug is gently rotated for a half circle until its lateral opening faces the opening of that arm of the U leading to the recipient's vein, whereupon the syringe is emptied.[4] Reverse rotation brings the plug's opening into apposition with the intake tube, whereupon the syringe is again filled only to be promptly emptied into the recipient by a half rotation of the plug similar to the first movement. In other words, the syringe draws up blood from an intake tube and empties it into an outgoing tube, the rotation plug acting as an intermediary between the two tubes.

A small metal ball attached to the plug facilitates its rotation, and another metal pin prevents its rotating more than a half circle by working in a specially constructed slot. Furthermore, the plug is ground into its pocket, and, though easily removable, fits

[3] These needles may be either sharp or blunt, and obturators go with each set. By this means, as soon as the needle is placed in the vein its lumen is closed by its obturator. All danger of clotting is obviated. When needles have been placed in both patient's and recipient's veins, obturators are removed and needles are attached to the tubing of the U tube.

[4] It is unnecessary to paraffin or coat with albolene any part of the apparatus.

so perfectly as to prevent entrance of air into the syringes. Worthy of note, too, is the fact that when

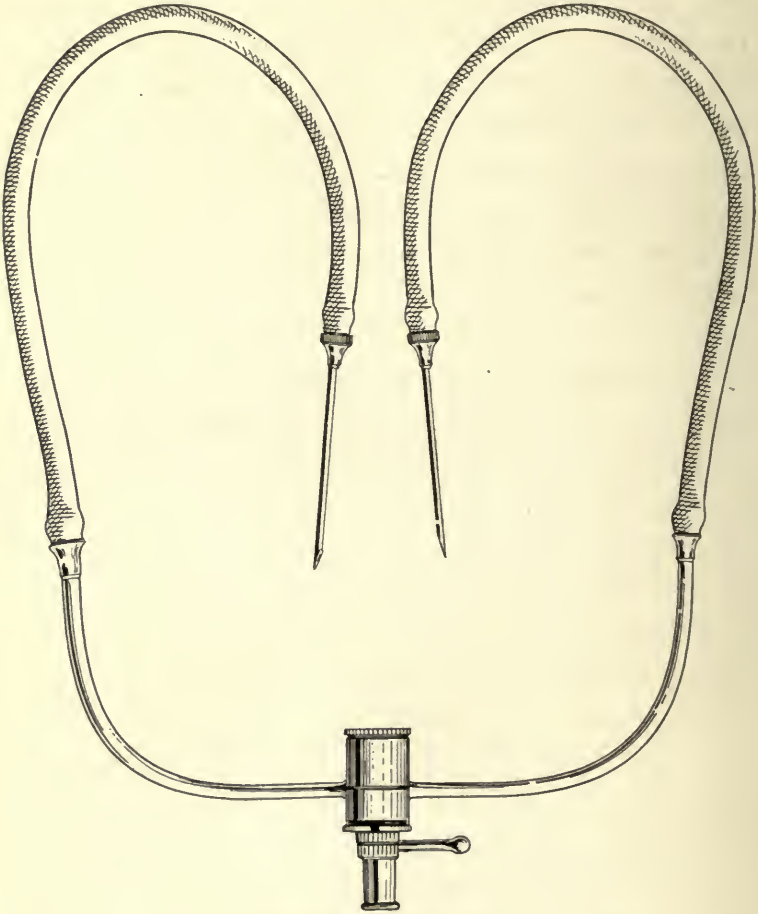

FIG. 16.—Author's U tube.

the lateral opening of the plug is "set" for one arm of the U, the other arm is effectually blocked, thus preventing any leakage.

In this manner successive syringefuls of blood may be withdrawn from the donor and emptied into the recipient with accuracy, precision and rapidity. And inasmuch as no syringe should ever be refilled more than two or three times without cleansing, it is quite simple as well as advisable to wash a few cubic centimetres of salt solution into each arm of the U as each fresh syringe is taken up. Thus clotting is avoided. Should, however, a clot arise or should it be necessary for any reason to discontinue the transfusion temporarily, the entire apparatus may be disconnected, washed out and held ready for resuming the operation."

Kimpton-Brown Method as Modified by Beth Vincent

" The results obtained by the transfusion of blood are probably less dependent upon the particular method employed than upon any other factor pertaining to the subject. The indications for a transfusion and the selection of the donor are more important than the technic of the operation. The therapeutic value of the blood is the same whether transferred by the citrate method as described by Weil and Lewisohn, with the glass cylinders of Kimpton and Brown, the pipette-cannular apparatus of Satterlee and Hooker, or by the syringe method of Lindeman. For this reason each surgeon should familiarize himself with the method which suits his own needs. The following method has been useful to me and may meet the requirements of other operators.

For the past three years I have used a glass tube or flask with a paraffin coating which inhibits the coagulation of blood and allows ample time to transfer it from donor to recipient. The tube resembles in principle and differs in shape from the cylinders described by Kimpton and Brown and the pipette of Satterlee and Hooker. This method is easy and practical and requires a skin incision to expose the vein in both donor and recipient which is not necessary in many cases.

Recently I have modified the tube so that it can be used with a needle of special design which obviates the skin incision on individuals with suitable veins. After a year's experience with the needle and the tube at the Massachusetts General Hospital and in my private work I find that this is the case with the donor, at least, in a large percentage of transfusions.

The tube is a cylinder with a capacity of 300 c.c., the upper end of which is closed with a rubber cork. About 3 cm. below the end is a side opening where connection is made with a bulb syringe which is used to express the contents of the tube. The lower end of the cylinder terminates in a glass tip, through which the blood enters and leaves the tube. About 2 cm. above the end of the tip is a ground-glass joint by means of which a tight connection can be made with the needle.

The needle is 6 cm. long and consists of a shaft and a socket of about equal length. The socket, which is the special feature of the needle, is made of an unusual depth so that there is no contact between the needle and that portion of the glass tip which projects into the socket below the ground-glass joint. The needle is made in two sizes, number 14 and 16 gauge. I find that I use the larger size in most cases.

PREPARATION OF TUBE AND NEEDLE

" The tubes are cleansed with hot water, wrapped in a towel with the cork and a short piece of rubber tubing and sterilized and dried in the autoclave. The process of coating the tubes with paraffin is then carried out under aseptic conditions. I have used 54 per cent. paraffin and various mixtures of stearin, paraffin and vaseline for coating and find that a commercial article sold under the name of " parowax " serves all practical purposes.

The paraffin which has been melted and sterilized in a metal dish is aspirated into the lower end of the tube and the outlets are covered with pads of gauze, while the tube is turned to make the wax run over all the inner surface. The excess of paraffin is allowed to run out at the tip, leaving a small amount in the tube to cover the cork when the tube is placed upon end to cool. This forms a disk of wax which makes

the cork air-tight, a condition which is essential to the proper use of the tube. As the tube cools a coating of paraffin appears on the inner surface. One should make sure that this covering is uniform and that the outlets are patent before the tubes are done up in sterile towels and put aside for future use.

The needles are cleansed, dried, and heated until sterile in a dish of melted paraffin. With sterile forceps a needle is then taken from the dish and the excess of wax is removed by shaking or by blowing air through the needle with a bulb syringe during the process of cooling to prevent the formation of a plug of wax in the lumen. The needles are then sterile and coated and can be kept in a sterile box until needed.

This process of coating the tubes and needles requires some practice and is bothersome to the surgeon. It is one of the disadvantages of the method, but the work can be delegated to any intelligent nurse. Prepared and put up in this way the needles and tubes may be kept indefinitely and are always ready for immediate use.

USE OF NEEDLE AND TUBE

"The method of using the needle and tube varies with the case to be transfused and the experience of the operator. The tube should be used without the needle in cases in which the veins of both donor and

recipient are small or hidden by a heavy layer of subcutaneous fat, or when the surgeon lacks practice in vein-puncture and is unable to enter the vein without causing a hæmatoma. Under these circumstances it is advisable to expose and open the vein through a skin incision and insert the tip of the tube directly into the vein as described by Kimpton and Brown. The blood is usually taken from one of the larger veins in the donor's elbow; while any vein in the arm or leg which will admit the glass tip can be used in transferring the blood to the recipient.

In most transfusions the veins of the donor are large and easy to puncture with the needle, while the veins of an anæmic recipient are apt to be small and hard to locate. For this reason it is usually advisable to take the blood from the donor into the tube by means of the needle, then disconnect the needle from the tube and inject the blood into the recipient through the glass tip which is inserted directly into a small vein previously exposed by skin incision.

Fig. 17 shows the manner of using the needle and tube to take the blood from a vein at the donor's elbow. The arm is prepared with iodine and a small amount of novocaine is injected into the skin over the selected vein which is made prominent by a tourniquet applied above the elbow. The application of the tourniquet is important; it should be placed directly on the skin

and adjusted by the operator so as to secure the maximum venous tension without stopping the arterial flow.

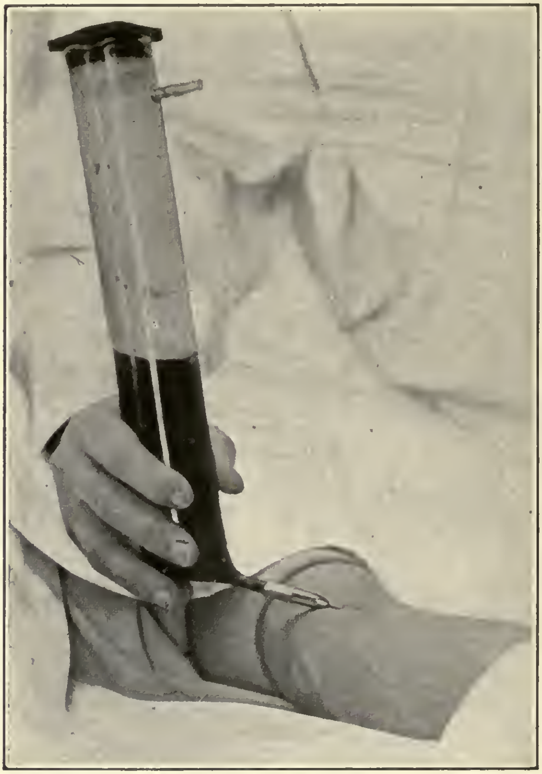

FIG. 17.—Shows use of needle to take blood from vein at the elbow. (*Surg., Gyne. and Obstet.*, November 5, 1916, vol. xxiii.

The needle is connected to the tube before making the puncture and inserted into the vein toward the wrist. As soon as the vein is entered the blood appears

at the bottom of the tube and steadily rises to the top by virtue of the pressure in the vein. The rate of flow is increased if the donor "works the fist" during the procedure. When the tube is filled, which usually takes three or four minutes, the flow is checked by releasing the tourniquet. This should be done before the needle is removed to avoid the formation of a hæmatoma. As the needle, still attached to the tube, is withdrawn pressure is made over the vein at the site of the puncture. The needle is then disconnected from the tube and rinsed in cold salt solution. During this time the tube is kept in a horizontal position with the tip up to prevent the escape of blood. To complete the transfer, place the finger over the upper opening of the tube to control the flow of blood, depress the lower end and insert the tip into the vein of the recipient.

The average transfusion requires at least 600 c.c. of blood. In most cases, if a hæmatoma does not form around the vein, it is possible to take two and sometimes three tubes of blood from the same vein by reinserting the needle through the original skin puncture. It is not necessary to use a fresh tube and needle for each transfer of blood. If cleansed immediately with cold salt solution they may be employed a second or even a third time in the same transfusion. A single tube and two needles usually

suffice for a transfusion, although one should always be prepared with at least two coated tubes and extra needles.

The combination of needle puncture for the donor and incision for the recipient is the practical method in most transfusions, but under certain circumstances it is possible to use the needle on both the donor and the recipient. In such cases after the tube has been filled with blood from the donor as already described a needle is inserted into the median basilic or median cephalic vein of the recipient made prominent by a tourniquet above the elbow. As soon as blood flows from the needle the tourniquet is loosened, the tube, filled with blood, is connected with the needle and the contents expressed by means of the syringe.

This needle and tube method without incision applies especially well to the infant with an open anterior fontanelle where the blood is injected into the superior longitudinal sinus as suggested by Helmholz.

In my last seven cases of hemorrhagic disease of the newborn I have employed this method with very satisfactory results. The blood is taken by means of the needle from an elbow vein of the father who usually serves as the donor. One-half a tube, or 150 c.c. of blood, is sufficient, as the amount required to transfuse these cases varies from 90 to 120 c.c. The infant is placed at the end of a table with

the head on one side, as shown in Fig. 18, and held firmly in this position by an assistant. The needle is inserted at the posterior angle of the anterior fonta-

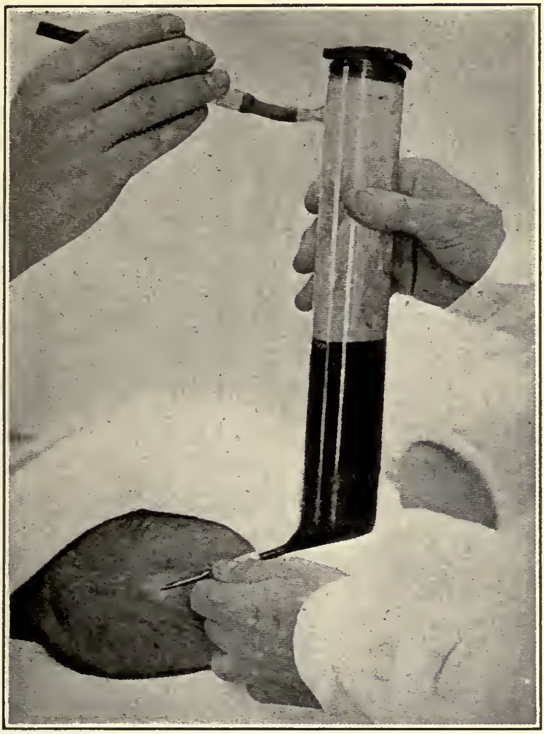

FIG. 18.—Shows position of infant's head and point at which the injection of blood is made into the longitudinal sinus.

nelle exactly in line with the sagittal suture. The sinus is just beneath the skin and dura and large enough at this point to be located easily even in a

new-born infant. As soon as the needle enters the sinus the fact is revealed by the flow of blood from the outer end. The needle is then held firmly in place while connection is made with the tube and the blood is slowly injected. The blood must be injected slowly to avoid a too rapid increase of intracranial pressure. In two of my cases this caused vomiting and disturbed respiration which corrected itself as soon as the flow of blood was checked temporarily. Air pressure in the tube should be released by detaching the syringe before the needle is withdrawn. There is no bleeding of any amount from the sinus even if the puncture has been made with a fairly large needle.

The chief disadvantage of this method of transfusion lies in the preparation of the needles and tubes but this process is not difficult and may be done in advance. The coated needles and tubes can be kept indefinitely and are always ready for immediate use. In practice the method is certain and flexible. The combination of needle and tube allows the surgeon to make a choice of procedures to suit his own operative experience and the need of the individual case. The tube with open incision is a sure method for any transfusion and under favorable conditions the use of the needle with the tube materially simplifies the operation."

Action of Sodium Citrate

Before giving the details of Lewisohn's method of using sodium citrate for purposes of blood transfusion, an understanding concerning the action of the drug in the body seems advisable. To this end the recent investigations of Salant and Wise throw much light on the subject and come at a peculiarly fortunate time. A summary of their views is as follows:

1. Sodium citrate is gotten rid of by the body in two ways: (*a*) oxidation by the tissues (not including the blood) into carbon dioxide and water as shown by Batteli and Stein and (*b*) through the kidneys. Apparently most of it is oxidized but a considerable amount (possibly 30 to 40 per cent.) is eliminated by the kidneys, the urine being made alkaline by the drug.

2. It disappears rapidly from the circulation after intravenous injection into cats and dogs. For example, 100 mg. of sodium citrate per kilo were injected into the femoral vein of a dog and about 60 to 70 per cent. disappeared in twenty seconds, while 10 to 20 per cent. of the remainder disappeared during the next five to ten minutes.

3. The oxidation and elimination are retarded when the doses are repeated and are probably much slower when large doses are given at frequent intervals.

4. Large doses given subcutaneously showed cumulative action.

5. The toxicity of sodium citrate when given intravenously depends to a large degree upon the rate of injection. This was proved by injecting a fatal dose rapidly and then giving the same dose to another animal very slowly. If the time of injection was extended over a really considerable period, such as two or three hours, a much larger dose could be withstood than had proved fatal in the first instance.

6. The toxicity of sodium citrate, aside from the rate of injection, depends upon the rate of its oxidation in the body, being more toxic for animals in which larger quantities are eliminated unchanged.

7. No after effects at all were observed from the use of sodium citrate. Neither sugar nor albumin was present in the urine which was examined for several days after toxic doses were administered. Symptoms developed rapidly, especially after large doses, and ended in recovery or death within a few hours. The action of the drug is therefore acute only.

8. Salant and Wise carried out all their investigations on animals, but Lewisohn, whose preliminary work was done with animals, determined that large amounts of a 0.2 per cent. solution of sodium citrate could be injected into a human without the slightest harm, and since citrate in this dilution will prevent

blood from clotting for two to three days, it is a most advantageous agent.

Lewisohn's Method of Sodium Citrate Transfusion

"The donor is put on a table, a tourniquet applied to the arm, and the vein punctured with a cannula. The blood is received in a sterile graduated glass jar (500 cm.) containing 25 c.c. of a 2 per cent. sterile solution of sodium citrate at the bottom. While the blood is running into the glass receptacle, it is well mixed with the citrate solution by means of a glass rod. After 250 c.c. of blood have been taken another 25 c.c. of citrate solution are added.[5] If less than 500 c.c. of blood are taken (*i.e.,* in infants), the amount of citrate solution added to the blood is reduced accordingly. In cases where we expect to take more than 500 cubic centimetres of blood we have another glass container (500 cm.) ready to be used in exactly the same manner. The glass jar containing the blood is then put aside and covered with a towel to safeguard against contamination. I have not found it necessary

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[5] Fifty cubic centimetres of a 2 per cent. solution of sodium citrate make a final dilution of 0.2 per cent. citrate when added to 500 c.c. of blood. But, since it is always advisable to have an excess of citrate, 450 c.c. of blood is a better amount to take than 500 c.c. to 50 c.c. of citrate. The clinical dilution therefore really amounts to about 0.25 per cent. rather than 0.2 per cent.

to immerse it in hot water or surround the jar with an asbestos covering. The blood is then taken either into the recipient's room or the recipient is brought into the operating room. I consider it a great advantage that this method does not require donor and recipient to be in the same room; this lessens the psychical shock of the whole procedure for the patient. In fact, the donor's blood may be collected in the laboratory or office and carried to the patient's bedside.

Another very great advantage of the citrate method is that as there is no connection between the donor and recipient, the donor is safeguarded against contagion of any disease or infection which the patient may have.

The recipient's vein is then punctured or exposed by a small incision; the cannula is introduced and attached to a salvarsan flask or a glass funnel. It is advisable to fill the rubber tubing connection between flask and cannula with some saline solution, so as to prevent air from getting into the circulation. After the connection is made the blood is poured into the salvarsan apparatus. In order to prevent sudden overloading of the circulation it is advisable (especially in larger transfusions) to stop the flow of blood from time to time by compressing the rubber tubing. After the blood has been injected the cannula is re-

moved and the transfusion is thus ended. The whole procedure can be performed with the greatest ease and without any hurry, because the citrated blood, as we have seen above, can be kept for two or three days in the glass jar without danger of clotting."

DISCUSSION AS TO THE MERITS OF CITRATED BLOOD FOR PURPOSES OF TRANSFUSION AS COMPARED TO WHOLE, UNTREATED BLOOD

While it is true that citrated blood will remain unclotted for forty-eight hours or more, there is some doubt as to the advisability of using it for transfusion purposes after it has been outside of the body any great length of time. Investigations concerning this matter are greatly to be desired, since it is possible that the cells may undergo some physiological or chemical change that would render them harmful when injected into the living blood stream—or at least unfit for carrying out the purposes for which they were intended. In a personal communication some months ago, Lewisohn rather advised against keeping the blood more than 24 hours. I have used it after a three-hour interval and would not hesitate to use it after six hours, but until more definite information is forthcoming, it seems to me best to maintain a conservative attitude. In fact, I can see little reason for keeping blood in bulk. Where the patient lives at a distance from the hospital or perhaps in a neighboring

city it would seem far safer to take the donor to the home instead of collecting the blood and carrying it in flasks; and where small, broken doses of blood are indicated, it is safer and simpler to take the amounts of blood from the donor as they are required rather than withdraw the entire quantity desired at one time and be compelled to keep it.

So far as can be determined there seems to be little difference between the therapeutic action of whole blood and citrated blood, although there should be a vast difference from a purely theoretical viewpoint. Since sodium citrate definitely inhibits blood coagulation outside the body, it would certainly seem that its intravenous injection should raise the coagulation time of the blood. If this were true, its use would be contraindicated in all forms of the hemorrhagic group of diseases and in the presence of active bleeding. The reverse, however, happens to be true. Instead of raising the coagulation time, according to Lewisohn and Weil, citrated blood lowers it for a time, after which coagulation time returns to normal. I have made no personal investigations on this point, but have proved by repeated clinical trial that its use in all forms of bleeding is attended with the same happy results as is that of whole untreated blood. For example, a 500-c.c. transfusion of citrated blood caused an immediate and permanent cessation of a profuse,

active hemorrhage from a gastric ulcer. A 55-c.c. dose of citrated blood brought about an equally satisfactory termination of bleeding in an infant one week old, who had had a family history of hæmophilia and took up the burden himself when he was circumcised. His condition was rapidly approaching the danger line. In another case, an obscure purpura, where a long series of transfusions were given, both of whole blood and citrated blood, the latter variety exerted equally as much influence on blood coagulation as the whole blood; neither brought about an entire stoppage although both caused a marked improvement. The results in other instances only reinforce the above conclusion. It seems paradoxical. I do not understand it, and Dr. Howell, to whom I have gone for an explanation, can hardly believe it possible that such is the case, but these are facts which have been repeated over and over again and always with the same result.

But there is one difference between a citrate transfusion and one in which whole untreated blood is used that cannot be passed over—a post-transfusion reaction, as manifested by a chill and fever, follows the citrate transfusion far more frequently than one with whole blood, and in cases where donor's and recipient's bloods match perfectly by every known test. Indeed, it is most unusual in my experience to have the slightest reaction after the whole blood transfusion

with perfectly matched bloods—even a rise of temperature of more than a degree or two is unusual. With the citrate blood, a violent chill and fever up to 103° or 105° is to be expected about 20 minutes after transfusion in about one out of every three or four cases and minor grades of the same sort occur even more frequently. This is most distressing to the patient and is unfortunate but it is of no consequence so far as the ultimate result is concerned, since it is unaccompanied by any blood destruction such as would be manifested by a hæmoglobinuria. In the light of Salant and Wise's work it may be due to the too rapid introduction of the citrated blood, but this is doubtful, since it has occurred after the slowest kind of transfusion and after the most elaborate care to avoid it. It is of citrate origin surely, but future investigation must reveal its true nature. One of the inexplicable features of this reaction is that its occurrence or nonoccurrence cannot be predicted. For example, I had occasion to do two transfusions on one patient and used the same perfectly matched donor for both. The interval was several weeks, the exact technic was used each time, the amounts of blood injected were identical and the quantity and strength of the citrate were the same. Not the slightest reaction followed the first transfusion, but a most distressing one followed the second, and great benefit accrued from both.

It is possible, even probable, that these reactions will be fathomed and eliminated, but since they are not actually harmful, and since the citrate method of transfusion has so many obvious advantages over all other methods, it seems to me, after careful comparison, to be the present method of election.

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CHAPTER VIII

TRANSFUSION FOR ACUTE HEMORRHAGE AND SHOCK. ACCIDENTAL GASTRIC ULCER. POSTOPERATIVE. POSTPARTUM. PLACENTA PRÆVIA. EXTRA-UTERINE PREGNANCY. TYPHOID FEVER

According to Bischoff, the blood of a human makes up about 7.4 per cent. of his total body weight and experiments on animals seem to indicate that a healthy individual could lose half of this amount and still recover without serious difficulty. With these figures clearly in mind, one might think it ought to be possible to gauge the extent of a hemorrhage and tell accurately when the borderline has been reached. And so it would be, perhaps, were it not for the unknown and unfathomable human factor that plays such a tremendous role in all illness. We do not know how much blood an individual can lose with safety because so many features enter into any computation that it is well-nigh impossible to take them all into account. Common report has it that the mother in child-birth can lose tremendous amounts of blood with impunity; certainly mothers do lose great

volumes and obstetricians, more than any other set of medical men, can sit idly by and watch a blood flow from the parturient woman that would appall his physician or surgeon brother. Perhaps the woman at term has more blood than at other times, more, possibly than her own body could use after her uterus has been emptied—but it is within the bounds of reason to suppose that the customary post-partum prostration might be less profound were the bleeding at parturition less profuse.

Whether it is true that at child-birth more blood can be lost than at any other time, or whether it is not, there certainly is absent at this time, in the great majority of cases, that one feature that plays the greatest part in determining how great or how little bleeding can be withstood—the psychic element. The woman in labor is fully occupied with her pains and the actual physical work she must perform; she has neither the time nor inclination to worry about a little thing like bleeding, which, even when it does come, she never sees. Practically always it occurs when she is at the end of her work, so tired and worn out that she really is not interested. The psychic element is totally absent—perhaps this accounts in a measure for her salvation.

What, then, is this psychic element? I confess I do not know. Shock is the common technical term

applied, but it fails utterly to explain this intangible complicating factor in our work. In certain instances it is partly compounded of fear, fear of impending death, but to claim that it is fear in every case would be unfair to that large group of individuals, who, against overwhelming odds, display an inspiring courage. There is no proof, in fact, in the assumption that the brave withstand blood loss better than the faint-hearted, although this is a tempting view to hold. I have often seen men, in whom there was not the slightest fear or anxiety as to the outcome, go utterly to pieces at a trifling hemorrhage, and I recall several instances of real cowards withstanding considerable loss. If a man has been caught up in a set of cog-wheels and flung around and around and has come out maimed and bleeding, he is quite naturally upset; his mental equilibrium has been profoundly deranged; that is quite understandable. But the man who has had an artery severed by a stray bullet or an accidental knife wound has encountered nothing more to shake his innermost mental workings than the sight of his own blood pouring out of his vessels, yet the same phenomenon of psychic disturbance may be encountered in him as was encountered in his mate of the cog-wheels—and neither may have had any fear in the least. Certain individuals are much more affected by blood loss than others; the size, age, social

status, *et cetera,* have little or nothing to do with the question. Quite naturally any accident will affect a man in ill-health more seriously than his robust mate, but that the big husky day laborer will stand an accidental hemorrhage better than the under-nourished, anæmic-looking clerk can never be predicted. I sometimes think it all depends upon the brain centres, especially the centre for blood-pressure, since it is a well-known fact that certain tissues can stand severe and prolonged anæmia much better than others, and of these, brain tissue is by far the most susceptible. The ordinary faint is an illustration of the dire consequences of even temporary depletion, the lowering of the head of the bed in all forms of fainting and bleeding being but the mechanical attempt to favor the circulation in the cranium. Certain it is that the psychic element, call it shock or anything else, is most intimately linked with the centre for blood-pressure, but which one is the most important or plays the primary rôle it is impossible to tell. The most one can say is—given a profoundly disturbed psychic base in cases of bleeding, a falling blood-pressure will result; given a psychic state of slight disturbance, a stable, though possibly somewhat fluttering, blood-pressure will be found—while a rising pressure portends a return to the normal mental state, although this latter statement can be put just the other way around,

namely a returning equilibrium will be accompanied by a rising pressure. Those who have worked in the field of transfusion will best understand the above discussion, while those who have seen isolated cases of hemorrhage may recognize certain phases similar to those encountered in their cases. The frantic attempts of relatives, friends, nurses and physicians to allay the fears of the injured or to quiet those suddenly seized with desperate illness, the white lies so glibly told to the dying that "All's well," "You're picking up wonderfully well," are our pathetic attempts to combat the depressed psychic condition which we know must be buoyed and lightened if restorative measures are to be, in any way, successful.

ACCIDENTAL HEMORRAGE

By accidental hemorrhage is understood those bleedings arising from wounds inflicted by any and all means—industrial accidents, stab wounds, bullet wounds, and such. Frequently, actual blood loss may not be so great as to cause the profound prostration exhibited by the patient, but investigation will reveal the fact that in many such cases the initial hemorrhage was quite sharp, so sharp in fact that it seemed as if death would ensue almost immediately. The patient fainted away—and thereby probably saved his own life! Rapid depletion, tremendous abrupt fall

in blood-pressure, anæmia of the brain, syncope, occasion a slowing of the blood current and absolute quiet of the patient, which more than anything else are conducive to clot formation at the site of the bleeding. Were it not for this sequence of events, I dare say the mortality from accidental hemorrhages would be more than double what it is to-day. Rapid loss of even comparatively small amounts of blood is of far more serious consequence than gradual loss of greater amounts, since in the latter case opportunity is afforded the vascular apparatus to adjust itself to conditions.

It should be an axiom among surgeons never to start a transfusion in accidental or other hemorrhages without first having controlled the original source of bleeding *if possible.* Failure to do this merely invites disaster, by pumping in and pumping out at the same time. There may, however, be instances where the condition of the patient is so precarious as to preclude an attempt to do anything. If such be the case, the best plan is to start the transfusion, and have everything in readiness to seek the source of the trouble the moment the patient picks up sufficiently to warrant such an attempt. By this means, many lives can be saved that otherwise would be lost. Practically none of the donor's blood will be lost, since it requires hardly more than 100 or 150 c.c. for a patient to pick up

sufficiently, and after the bleeding point is caught the transfusion may be continued to its logical conclusion. Oftentimes the wound is of such nature that prolonged manipulations are necessary to secure the bleeding point and more blood may be lost during them, in which case the donor's blood had better be conserved. This can only be done by an interruption of the transfusion from time to time, and resuming it as the patient's condition demands, for which purpose the two-tube method of direct transfusion which I devised some years ago is especially well adapted, the usual methods of indirect transfusion being unsuited because of the likelihood of clot formation in the needles during the intervals. The citrate method, though, may be used for this purpose, and possibly may prove to be the method of election.

Up to this time I have been speaking of cases of massive bleeding which is still in process, but there is a far greater class which must be considered and in which the keenest judgment is required. Many cases arise where the bleeding has been quite severe and the patient comes in in evident distress although the source of the hemorrhage has been controlled. Is a transfusion necessary, or is it not? A more difficult question could hardly be propounded. Where there is air-hunger, I proceed at once to transfusion; it may be that supportive treatment would save the day—in

fact, I know of cases where it did—but the margin of safety has been strained to the uttermost limits whenever air-hunger is in evidence, and I prefer not to trifle with it. I have seen several fatalities because of the delay incidental to the carrying out of supportive measures. However, cases of air-hunger are relatively uncommon and really offer little difficulty so far as judgment is concerned.

Volcanic gastric ulcers, placenta prævia, typhoid bleeding and allied conditions at times offer most difficult problems in diagnosis, prognosis and judgment. I have heard the statement made that no one ever bleeds to death from a gastric ulcer and certain gynæcologists maintain that a fatal ending never results from the hemorrhage of a ruptured extra-uterine pregnancy, both of which statements have done incalculable harm. There is no form of bleeding known which cannot, which does not, at times, result fatally, however insignificant its inception may have been. I have personally seen several deaths from bleeding gastric ulcers, from ruptured ectopic pregnancies, from intestinal hemorrhages in the course of typhoid fever and from a number of other hemorrhagic conditions that are thought to be non-fatal by many men who have accepted unfounded assertions without investigation. I will admit that acute hemorrhages do not culminate fatally in the vast majority of instances,

but many of them progress so near to a fatal issue that any prediction as to the ultimate end of an actual fulminating bleeding is one of the most foolhardy things I know of. The saving mechanism, of course, in these affairs is the automatic fall in blood-pressure with consequent relief of tension and slowing of the blood current, which favors clot formation at the site of the bleeding. But who can tell whether the vessel at fault is vein or artery, large or small? And what is to be the deciding point in choosing a course of action—shall we allow the bleeding to proceed to practical exsanguination with great risk involved, or shall we resort to supportive measures and if so—what, and when?

Certain measures should be adopted in all acute hemorrhages because certain features are common to all of them, the chief points of difference being due, generally speaking, solely to the anatomical location of the affected vessel and its supporting tissues. An artery is an artery whether it is in the stomach or the kidney, and, when it is injured, bleeds the same way in either place, and with equal harm. But the tissues surrounding the stomach artery are very dissimilar from those surrounding the renal vessel, or those surrounding a uterine artery, and the future course of a hemorrhage may depend a great deal upon these anatomical differences.

Therefore rest, sedatives, an ice-bag over the bleeding area if accessible or convenient (the idea being to favor contraction of the blood vessels), elevation of the foot of the bed to avoid brain anæmia, plenty of water to quench the thirst, bandaging the extremities, perhaps, and a slow infusion of a moderate amount of salt solution to maintain a semblance of blood bulk, to steady a faltering blood-pressure and to relieve thirst, these and other less used measures are common to almost any form of hemorrhage. Packing or ligating any accessible vessel comes in the same category, after which general remedies, the course of treatment is differentiated.

GASTRIC ULCER

In a subsiding gastric hemorrhage it is wise to restrict the liquids in order to keep the blood bulk as low as possible, but, if the case has proceeded almost to exsanguination, it is advisable to give slow salt, or sugar solution per rectum, or a slow infusion of not over 500 to 1000 c.c. One must always be on guard, though, in concluding that any gastric bleeding has subsided or is subsiding. The weaker a patient gets and the lower his blood pressure, the slower is the bleeding and the longer does it take the stomach to fill up; the warning nausea, too, is less pronounced and vomiting of contained blood may not take place until the stomach becomes full to overflowing.

It would take me too far afield to discuss the pros and cons of gastro-enterostomy or pyloroplasty or simple resection or scarification of an ulcer for bleeding. Ligation of a bleeding point is absolutely the surest way of stopping hemorrhage, but there are times when it is neither the safest, surest nor wisest thing to do. I have seen cases of gastric bleeding where prompt exploration and gastro-enterostomy gave brilliant results, and I have seen cases where a saner judgment might have decided against the operation which ended fatally. For the purpose of this discussion, I can only say that with a patient *in extremis* from bleeding, transfusion before, during or immediately after operation considerably enhances the chances of success. The first patient I ever transfused was of this type and several subsequent cases have done equally well. Even when the patient is not exsanguinated, it is wise to have a suitable donor on hand in case of emergency.

Finally there is a group of gastric cases in which for one reason or another operation is out of the question. In these and in all other forms of apparently intractable bleeding where all the usual measures to stop it have been unavailing, I make it a fixed rule to do a blood transfusion if the blood-pressure reaches 70 mm. of mercury, and not infrequently I transfuse

with the pressure around 100 mm. The rate of inflow in these cases must be carefully guarded, and the amount of blood given rather small, for fear of raising the pressure too suddenly and too high, thus exciting renewed bleeding. In the last case 500 c.c. improved the patient's condition markedly and a prompt cessation of the bleeding took place, but I think 350 or 400 c.c. is a safer quantity to give. It is too much, perhaps, to expect a large artery to cease pouring out blood by a simple transfusion, but one rarely has a chance to do a transfusion where a really big vessel is open, and where the smaller ones are at fault a slowing of the current has already taken place before the transfusion is started. In all those cases that I have done, except the actually moribund, the bleeding has stopped with the accession of new blood. In one it started up again one month later but stopped permanently with a second transfusion. Just why it should stop is problematical, but we know fresh human blood exerts a beneficial effect on coagulation in any and all forms of bleeding. Hence experience has shown that when all other means fail, blood transfusion, properly managed, should be tried. Even in those cases where the bleeding has ceased, it is at times advisable to transfuse because of the profound prostration, and at a later stage one or more transfusions may be indicated to relieve the severe anæmia and to give a fresh start in the upbuild-

ing process. Especially is this so in those cases of repeated hemorrhages where the blood forming organs have been called upon so often that they finally fail to respond. A case in point is that of a nurse who became chronically anæmic and prostrated from several gastric bleedings. Rest in bed, forced feeding and drug therapy utterly failed, but two transfusions gave her a new lease on life and her hemorrhages have not recurred. She is now in perfect health and actively engaged in her profession.

INTESTINAL BLEEDING

The intestinal hemorrhages differ little from the gastric ones. Usually encountered during the course of typhoid fever, most of them cease spontaneously when the pressure falls, but they tend to recur when it rises. Some of them, though, do not cease and the old question of procedure arises. It is so difficult to distinguish between benign and dangerous intestinal hemorrhages. With the advent of sodium citrate transfusion, and its more thorough comprehension, it seems likely that transfusion will be considered as indicated in more cases of typhoid bleeding than is at present the custom, especially if an immune donor can be found. The disease itself is bad enough and it has been a mystery to me how any of these cases recover after the debilitating influence of the terrific hemorrhages so frequently seen. At present it is

rather uncommon to transfuse these cases, because of the necessity for disturbing them and the consequent danger of making matters worse. I have done but one case and that one had perforated in addition to having had several hemorrhages. In spite of his moribund condition, he withstood operation fairly well and lived four days, but was too weak to survive.

POST-OPERATIVE BLEEDING

I have considered the differential diagnosis of post-operative hemorrhages rather in detail in Chapter II. In the present connection, it is, therefore, sufficient to say that where a correct diagnosis of the trouble has been promptly made, it usually suffices to open the wound, find the bleeding point and tie it. The patients are always badly shocked, but generally respond to rest, warmth and salt infusions. A case in point occurred in November, 1916. A woman had undergone an extensive pelvic operation and was returned to her room in good condition. Suddenly, four or five hours later, her nurse was astonished to find her pulse very rapid and irregular, her face blanched and respirations rapid and shallow. The cause was evident in the blood that was pouring out of the vagina along a drain. Prompt reopening of the abdominal incision revealed considerable blood in the lower abdomen, the source of which was the uter-

ine stump. A few sutures stopped the bleeding and the patient was returned to her bed to undergo a somewhat delayed but satisfactory convalescence. Her condition improved the moment the leakage was stopped and a salt solution infusion did the rest.

Time ought never be wasted in attempting to stop a post-operative hemorrhage by means other than reopening of the wound and catching the bleeding point. Extraneous blood in the peritoneal cavity can do no possible good and the formation of an hæmatoma in any wound only encourages infection. Where the bleeding has escaped detection or has been so excessive as to preclude reopening of the incision, I have urged and repeatedly carried out transfusion, during the course of which the secondary operation has been successfully done. The method of procedure is to take the patient to the operating room and start the transfusion, either direct or indirect but preferably the former, under local anæsthesia. With the introduction of comparatively little (hardly over 150 c.c.) of fresh blood the patient invariably takes on renewed life and the blood-pressure rises. The moment this stage is reached ether is started—always ether because of its stimulating effect on the heart action—and with light but full anæsthesia the wound is opened. During the course of the manipulations necessary to find, secure, and tie the offending vessel or vessels the

transfusion is interrupted, since to continue amounts to but little more than wasteful pumping in and pumping out at the same time. But the moment the bleeding point is secure, the blood flow is again started and carried to its conclusion. Some of the most brilliant results imaginable have been secured in this type of case. One of these was that of a woman who suddenly collapsed a few hours after an extensive abdominal operation during the course of which the appendix and gall-bladder had been removed. During the course of a transfusion the abdomen was reopened and found to be filled with blood which was coming from the cystic artery which had slipped its ligature. It was secured, the patient was given a little extra blood to make up the loss and a satisfactory convalescence ensued. Another was a kidney case where, after a nephrotomy for stone, sudden bleeding took place of such severity that the wound had to be reopened and resutured, an undertaking that would have been impossible in this instance without coincident transfusion. Still another was bleeding after a gastro-enterostomy. These and others go to form a most satisfactory series.

RUPTURED ECTOPIC PREGNANCY

Ruptured extra-uterine pregnancy, of which I have spoken more in detail elsewhere, should be handled exactly like a post-operative hemorrhage.

Where the patient's condition warrants, which is in the majority of cases, prompt operation should be done. Where there is some doubt concerning the ability to stand interference, rest, sedatives and a slow infusion of moderate amounts of salt solution will occasionally bring back a woman sufficiently to withstand operation. In order to do this the greatest care and judgment must be exercised and the operation should be done as soon as the patient strikes the upgrade, because it occasionally happens that the improvement is fleeting and unless the opportunity is grasped the moment it presents, the chance is lost, for a second opportunity comes but rarely. Those cases which fail to respond or which are so profoundly shocked as to preclude supportive measures should be immediately transfused, and operated on, as outlined under post-operative hemorrhage. A case of this type occurred in my practice not many months ago. A young married woman, patient of Dr. E. H. Richardson, suddenly had an excruciating pain in her lower abdomen while at stool. She fainted and a little later her physician diagnosed ruptured extra-uterine pregnancy and sent her to the hospital where an attempt was made to relieve her from a dangerous state of prostration. After two or three hours a slight improvement came to pass, but it was extremely fleet-

ing, and she shortly afterward became definitely worse. Transfusion and coincident operation were followed by a perfectly normal convalescence.

POSTPARTUM BLEEDING

It has been my fortune to be called upon in a number of postpartum hemorrhages and as a result of the experience thus gained, whenever an obstetrician calls for help, I always know that there is no doubt of there having been a real hemorrhage, for of all medical men, obstetricians are the most complacent in the face of conditions that are, to say the least, trying. This attitude is doubtless essential to the make-up of a successful obstetrician, since it would obviously be rather harrowing for him to be upset at the sight of considerable amounts of blood—a bloodless delivery is unknown—but I sometimes feel that a certain degree of sensitiveness would be to his advantage. Every case I have seen has been practically exsanguinated, several being absolutely beyond hope by the time I arrived.

But the obstetricians are not only complacent in the face of danger, they are the most optimistic set of men imaginable. They are so accustomed to witnessing a prompt return to well-being after profuse bleedings that the slightest improvement gives them inordinate satisfaction and comfort, so much so that

they are prone to delay matters until their patient is actually *in extremis*. I have lost two or three patients by taking stock in their superior knowledge of post-partum hemorrhages, when my own judgment urged a most hurried transfusion, so that now I proceed along the theory that if an obstetrician really considers a transfusion he must have been at least a bit frightened, and if the bleeding was sufficient to frighten him, it must have been a terrific hemorrhage. And since adopting this course, my results in obstetrical bleedings have been better. I transfuse without delay nearly every one I see. In two instances, though, bandaging the extremities, salt infusions, uterine massage, packing, rest and morphine sufficed.

From all I can gather the chief cause of post-partum hemorrhage seems to be atony of the uterus resulting from prolonged labor, dystocia, and high forceps. Whether these are actual causes or merely incidental, I am not prepared to say. Another factor, possibly it is the primary one, is the failure of ergot or pituitrin to bring about uterine contractions. I frequently find that during the labor it has been necessary to mechanically dilate the cervix, always a procedure that causes great shock. The story is, that with the oncoming of intractable bleeding the uterus was packed; this stopped the bleeding to a certain extent, but it seemed to add still further to the shock,

either by stretching an organ that was trying, or should have been trying, to contract or still further dilating the cervix or keeping it dilated when it ought to have been getting smaller, a question for the obstetrician to decide.

In one striking case, the consulting obstetrician, Dr. J. M. H. Rowland, felt that the bleeding was coming entirely from a deeply torn cervix, but the patient was in such a precarious state that he dared not touch her. During the course of a transfusion, though, he removed the packs, verified his diagnosis and repaired the damage. The patient improved wonderfully as soon as the packs were removed; therefore since the bleeding source had been controlled, they were not replaced. A normal convalescence ensued. In another case, that of Dr. Carl Wilson, the patient was markedly improved by transfusion, but she had lost so much blood that it was deemed unwise to touch the packs at that time. Half of them were removed on the following day and the remainder on the third day without further bleeding, the patient making a good recovery.

PLACENTA PRÆVIA BLEEDING

Of all the obstetrical hemorrhages, the placenta prævias are the saddest, because the child is frequently lost and the mother either has a narrow escape or is lost too. It has been my good fortune to have saved

a few mothers by prompt transfusion—but I must chronicle one death, that of a primipara who, after bleeding for two weeks off and on, was withheld from delivery by an experienced obstetrician in order to give the child a better chance for life. One morning the hemorrhage became quite profuse and a hurried delivery by version was done, as a result of which the child died, but the mother seemed to be all right. Five hours later an apparent atony of the uterus ensued which was heralded by a terrific gush of blood. When I arrived the most harrowing air-hunger was in evidence and I attempted a rapid transfusion, but it was only another one of those cases which must go on the records with the comment of "too late" opposite the name.[1]

In one instance where the bleeding had been in progress for some hours and the patient seemed to be in very bad condition, I started a direct transfusion and revived her to such extent that it was safe to etherize her, whereupon, the blood still pouring into

[1] This type of blood loss might well be termed "Cumulative Bleeding" since it is the repeated small blood losses spread out over a considerable period that place the patient in such weakened condition, frequently unsuspected, that a final sudden sharp hemorrhage proves disastrous. Ordinarily this last hemorrhage would not be considered really alarming were it not for the "Cumulative effect" of the previous bleedings.

her veins, the obstetrician did a hurried version and extraction, and one life at least (the mother's) was saved. In another case transfusion immediately after delivery made up the blood loss, and both mother and babe were saved.

There can, of course, be no absolute routine for these cases because many of them are delivered by the ideal Cæsarean section and run little danger so far as bleeding is concerned. But it does seem reasonable to suggest preliminary preparations for transfusion in those instances where Cæsarean section is not to be done and where bleeding has been going on for some time, and where the patient is in bad condition. The maternal mortality will thus surely be reduced. Preliminary blood tests and preparations for transfusion would be especially helpful in those instances of known placenta prævia where attempts are being made to carry the mother along in order to get a viable child.

PREMATURE SEPARATION OF THE PLACENTA

I have done a transfusion in still another form of obstetrical bleeding, though a most rare one. It was an instance of premature separation of the placenta in a woman eight months pregnant and previously well. At operation by Dr. J. Whitridge Williams a tremendous quantity of blood was found in the uterus,

which, after being emptied of its dead incubus, utterly failed to contract and had to be removed. The patient was terribly exsanguinated, but with careful handling seemed about to come back, when, seventy-two hours after operation, she took a turn for the worse, and seemed in such imminent danger that a transfusion was done. Her recovery after that was slow but uneventful.[2]

From the foregoing survey, it will be apparent that blood transfusion may be of service in a number of different varieties of acute blood loss if judiciously employed. The most difficult feature in connection with it seems to be not where it should be used, but when, and it may, perhaps, be in order to suggest that the best results will be obtained in those cases where the patient has not been allowed to proceed too far in the bleeding course. No one realizes better than I the difficulties encountered in deciding just when the actual limit of bleeding has been reached, and for that reason it seems that one ought never wait for the actual limit of endurance. Only too often a bleeding patient will actually be, or seem to be, in good shape almost to the very end, thus rendering accurate judgment all but impossible. A stable

[2] Since writing this I have had another similar case, that of Drs. Dobbin and Bergland. Transfusion and Cæsarean section saved the mother.

blood-pressure that is well within the limits of safety will sometimes take a tumble from which it never recovers. Acute hemorrhage from any cause is a dangerous thing; it ought never be trifled with; at times it ends with great unexpectedness, once and for all.

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CHAPTER IX

TRANSFUSION FOR ANÆMIC AND DEBILITATED CONDITIONS IN GENERAL. BLOOD DOSAGE

UNEXPLOITED as the purely secondary anæmias now are, I venture to predict that they will eventually play a conspicuous part in developing blood transfusion therapy to its fullest usefulness. Up to the present only those conditions have been subjected to transfusion that have demanded it as a common sense procedure or were of such character that nothing of a known nature could help and something in the nature of the unknown was deemed permissible as a trial. Many reasons suggest themselves as the cause of this, chief among which was the previous technical difficulty of carrying out a transfusion, a state of affairs that has now happily been overcome.

In June, 1913, I read a paper before the American Medical Association, then meeting in Minneapolis, entitled, "Therapeutic Possibilities of Transfusion," during the course of which I asked these questions: "Is transfusion purely and simply an emergency operation? May not its chief field of usefulness be rather as a therapeutic agent, and have we not almost entirely overlooked this possibility?" Cer-

tain predictions were then made, notably the further and continued use of transfusion in pernicious anæmia, and it was suggested that many secondary anæmias might be tremendously helped by the addition of fresh blood, especially in the case of those whose path back to health was so slow and circuitous. I argued that transfusion would give an irrepressible impetus to many individuals whose debilitated, anæmic body had all but ceased to respond to the usual treatment of rest, fresh air, diet and the variously used drugs.

Subsequent events have proved my contention, as is evidenced by the continually expanding field of blood transfusion therapy, but certain features connected with it are still unrecognized and much more remains to be done, chiefly the education of physicians to a realization that chronic secondary anæmia is a distressing, serious condition which demands for its relief more than renewed, interchangeable prescriptions and a little rest. Our present day therapy differs but slightly from that in vogue years and years ago—rest, forced feeding, iron, arsenic, etc.—in fact about the only real change is in the arsenical preparation now used; the cacodylates have supplanted Fowler's solution in the affections of most physicians. The thought seems never to occur that anæmia means blood loss, blood depletion, and that the best way of

supplying the deficiency is to actually put new blood into the unfilled veins.

If a woman suffers repeated hemorrhages from uterine fibroids, she is put to bed for two or three weeks in order to get into condition for an operation, and if she refuses to be operated on she is put to bed and treated in the same way anyhow. Or if her medical attendants are a bit careless, she may be operated on without the building-up process—so many women have come through pelvic operations in spite of profound anæmia that it is rather common to disregard it as a real menace. Convalescence might be rather stormy in some and rather prolonged, but they get well, so why bother?

In certain of the intestinal bleedings, many of obscure origin and perhaps not amenable to surgical intervention, how the poor patients are put through rest cure processes, not once but repeatedly, until there finally comes a time when the poor blood-forming organs simply refuse to build, in spite of pharmaceutical lashings prolonged and various—pale, thin, weak individuals, unable to sleep, unable to eat, fearful of another hemorrhage perhaps, desirous of performing their wonted tasks but physically unfit, always tired and discouraged, a burden to themselves and their relatives and friends. Certainly they cannot eat, and what little food does pass their lips is tasteless.

The colorless tongue denotes tasteless food and an anæmic state. It is always so in anæmia, and the appetite changes only when the blood picture changes.

There are many other individuals, notably those cases of chronic illness, who finally come to operation or exploration, not because they have been diagnosed, but because they have remained ill, all efforts to the contrary notwithstanding, and a delayed surgical investigation suggests itself as the only remaining avenue of hope. These are very bad surgical risks, for whom a transfusion, prior to or during operation, would enhance the chances of recovery and provide a shortened, tranquil convalescence in place of the precarious one almost surely to be encountered without the addition of new blood. In a paper entitled "Blood Transfusion, Indications and Results, Based on Observations of 212 Transfusions," Libman and Ottenberg call attention to this class of cases, saying, "Among the most satisfactory transfusions in the whole series were some of those done preliminary to operation in patients whose desperate condition would otherwise have contra-indicated any other operation. There were 23 pre-operative transfusions and in 13 of them the result was decisive and the patient recovered."

There is another group, for whom post-operative transfusion would be an invaluable aid—cases whose convalescence is stormy and delayed although the con-

dition at operation may have been quite satisfactory. The shock has been too great, an accident has happened or a post-operative prostration quite unwarranted by the condition prior to operation has ensued. Instead of two or three weeks in the hospital, the visit lengthens to five or six weeks for these cases, and the building up process may even have to be continued at home. Those who apparently cannot come back after operation under ordinary treatment can do so in many instances if given a little blood. Peterson reports such a case, the patient being a little boy who had had a pneumonia during whose course an empyema, for which he came to operation, developed. He ran a very high temperature, gradually lost weight and strength, refused all nourishment and, to make matters worse, developed a diarrhœa. No pocketing of the empyema cavity could be discovered, and the case was considered hopeless, when as a last resort it was decided to try blood transfusion. With the mother acting as donor, 235 c.c. of blood was transfused, and from that moment the child began to improve. His temperature dropped immediately, remained down, and an uninterrupted recovery ensued. Could anything be more illuminating?

Another instructive case, one of my own, is that of a man who had had a gastric resection for carcinoma. In bad condition prior to operation and quite anæmic, his post-operative course was steadily downward. His

wound broke down, he was unable to take or retain nourishment, and he began to run a temperature very suggestive of a deep-seated infection. His red cells numbered 1,900,000, while his hæmoglobin was 21 per cent. He was pale, desperately weak, absolutely without hope, and he had the anxious expression, the cold clammy skin so characteristic of those in utter prostration. I gave him 500 c.c. of citrated blood, and three days later he had a red count of 3,260,000 cells and a hæmoglobin of 31 per cent., while his temperature had changed its type, and was running a rather irregular course around the normal base line. His wound, too, began to take on renewed vigor, and the man himself began to look about. But the work was not finished. In order to clinch matter, I gave him another smaller dose of blood eight days after the first, and from that moment on, his convalescence was rapid and uninterrupted.

Other examples abound, but these foregoing are sufficient to indicate the necessity for an awakening on the part of physicians and surgeons to certain definite deficiencies in their handling of anæmic debilitated states. They have failed to recognize the benefits held out in the form of blood transfusion. If a person suffers a sudden loss of great volumes of blood, we make up the deficiency by adding fresh blood. Why, then, do we not do likewise in the many

secondary anæmias that also suffer blood losses but in smaller amounts and over longer periods? Why persist in keeping these people incapacitated when a transfusion will help them so tremendously? How can an ulcer heal when there is not blood enough to allow its base to become healthy? How can a patient eat when everything is tasteless and the very sight of food produces nausea? Of what use is the food when it reaches the stomach, if there is not blood enough to take it up, if it simply putrefies and turns to gas and causes the distressing distention of anæmia? I have transfused a few of the chronics, and the new blood has done more to restore hope and sleep and appetite than weeks of rest and barrels of iron and arsenic. I do not decry these necessary adjuvants in the least; on the contrary, I advise their constant use and have seen splendid results obtained. I merely deprecate and condemn their promiscuous employment in conditions beyond their therapeutic reach. They can do a certain amount, but in many cases they are absolutely worthless, and in many of these one or more transfusions will almost produce a miracle, after which the drug and rest therapy may be judiciously resumed. This has been proved but it has not been recognized.

Thus it will probably come to pass that the aid of blood transfusion will be invoked as the usual thing

in many conditions where its use at the present time is decidedly a rarity, and almost of the experimental variety. This will be a definite advance in many ways, particularly as regards our knowledge of *blood dosage,* a matter that hitherto has been almost totally neglected for reasons quite obvious. As matters stand now, we give from five to ten, or even twelve hundred cubic centimetres of blood in cases of actual voluminous blood loss, the exact amount depending almost entirely upon the ability of the donor to stand the depletion. Lesser amounts are transfused where the blood loss has not been so great, and to a certain extent, in those conditions of impaired coagulation apparatus. The conviction is prevalent that comparatively small doses of blood are advisable in pernicious anæmia rather than massive doses, which seem to overdistend the vessels, cause a marked sense of discomfort, and stimulate the new blood formation rather less actively than the smaller doses. It has always been understood that the amount of blood transfused should be small in the presence of actual bleeding of any character, intestinal or otherwise, where surgical control is not feasible or not to be attempted. But these differences in dosage are often very gross. An average size dose, I should say, is about 500 c.c. of blood, a very considerable amount, and one that cannot be given up or taken in without serious consideration of every phase of the

case. Future experience may teach that much smaller doses given at definite periods will prove more efficacious in certain conditions. Twenty-five cubic centimetres could be placed into a patient's veins three times a day without the slightest difficulty, now that we have the citrate method of transfusion, and it may be that a course of such treatment, extending over a week or two, will come to be the routine for some of the anæmias. In others, 50 c.c. a day for ten days may be sufficient or 100 c.c. every other day, the idea being to use blood as a stimulant or perhaps even for its nutritional value, instead of giving it in bulk as is now customary. A husband, brother, or sister could give up these insignificant amounts of blood each day, or every two or three days, without inconvenience or harm, and it may even be proved that hæmolytic and agglutination tests will prove superfluous, since the amounts given would be so small as to be incapable of causing serious trouble.

These matters are not capable of animal experimentation, and I can do no more than suggest these possibilities, leaving it to the medical men to develop them. The time has arrived when we should seriously begin to study *blood dosage* and *therapy.* We must know definitely when massive doses should be used, when smaller doses would be advisable and when what I shall term therapeutic doses would seem to be indi-

cated. Perhaps some of the conditions that now fail to yield to the larger gross doses of blood might be greatly benefited and even cured by small therapeutic amounts extended over a longer period. There are many aspects to this problem, which should all be investigated and explained. Rapidly as the advance in blood transfusion has taken place, and brilliant as the achievements have been, it must be admitted that some of its phases still remain in a very unsatisfactory state. We have been so absorbed with the technical details that others, less important but not less interesting, have been neglected.

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CHAPTER X

PRIMARY PERNICIOUS ANÆMIA

During the last two or three years much attention has been directed to that condition known as *primary pernicious anæmia,* and a voluminous literature has arisen as a consequence, all of which came about following the investigations of Eppinger, Decastello and Klemperer, who, working independently, became convinced of the great good that might come from the removal of the spleen in pernicious anæmia. It is worthy of note that Eppinger was led to adopt this procedure by observing after splenectomy a diminished output of urobilin and other instances of decreased hæmolysis, while Decastello noted the improvement that followed splenectomy in the related conditions, hæmolytic jaundice and Banti's disease. Klemperer was influenced by the clinical observation that splenectomy for such conditions as rupture of the spleen was in some instances eventually followed by polycythæmia.

Following the work of these three investigators whose cases apparently did wondrously well, the procedure of splenectomy was at once seized upon almost throughout the entire civilized world as a new and successful means of combating what had hitherto been

considered a most refractory condition, so that in the short period of two and a half years a fairly large number of cases has become available for study. At first certain of the cases were splenectomized without sufficient care in preparation—the operation being haled with such enthusiasm that little consideration was accorded the *actual surgery* necessary to the removal of the spleen. Many of these cases, naturally, promptly died as a result of the operation, whereupon the custom arose of either treating all cases of pernicious anæmia by the usual methods of drug therapy until they were in a suitable condition for operation or, when this was not possible, transfusing them one or more times until such a state of affairs came about. Under this régime, the mortality of the operation has been markedly reduced and it has been possible to really study the effect that splenectomy might have on the course of the disease.

Idiopathic or primary progressive anæmia was characterized by Addison who first clearly described it as " a general anæmia occurring without any discoverable cause whatever; cases in which there had been no previous loss of blood, no exhausting diarrhœa, no chlorosis, no renal, splenic, miasmatic, glandular, strumous, or malignant disease." It affects middle-aged persons chiefly, but instances in young individuals and in children have been described. As its

name signifies, it comes on without previous illness, although in many cases there is a history of gastro-intestinal disturbance, mental shock, or worry, and (according to Addison) "It makes its approach in so slow and insidious a manner that the patient can hardly fix a date to the earliest feeling of languor which is shortly to become so extreme. The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted, the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement. There is an increasing indisposition to exertion, with an uncomfortable feeling of faintness or breathlessness in attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth and waxy appearance; the lips, gums and tongue seem bloodless, the flabbiness of the solids increases, the appetite fails, extreme languor and faintness supervene, breathlessness and palpitations are produced by the most trifling exertion or emotion; some slight œdema is probably perceived about the ankles; the debility becomes extreme—the patient can no longer rise from bed; the mind occasionally wanders; he falls into a prostrate and half torpid state, and at length expires; nevertheless, to the very last, and after a sickness of several months' duration the bulkiness of the general

frame and the amount of obesity often present a most striking contrast to the failure and exhaustion observable in every other respect."

The red blood-cells show a progressive decrease in number and may fall to one-fifth or one-tenth of the normal number in extreme cases, while the hæmoglobin falls in proportion, although this latter feature is relatively increased as is indicated by the color index which, in typical cases of pernicious anæmia, is plus one, a condition exactly opposite to that which occurs in secondary anæmia, in which the corpuscular richness in coloring matter is decreased, the color index being minus one.

It has always been understood, and in the light of recent investigations correctly so, that the trouble has been the destruction of the red cells rather than a failure upon the part of the blood-forming organs to produce those cells in quantities sufficient to meet the needs of the organism. This is very well shown by the appearance in the blood of those suffering from pernicious anæmia of the characteristic forms of unfinished blood-cells, the normoblasts and megaloblasts, the presence of which is interpreted as indicating a demand upon the blood-forming organs for red corpuscles faster than they can be produced, the result being that an incomplete nucleated product is to a certain extent turned loose into the circulation. As a

rule only a small number of these cells are to be found, but upon certain occasions known as blood crises they occur in myriads, or what is technically known as "showers," the exact significance of which is obscure, although it is commonly considered to be due to an excessive stimulus of some nature to the hæmatopoietic organs.

In the true case of pernicious anæmia, the outlook is exceedingly bad, although many cases have been helped by treatment with the various arsenical preparations, some even coming back almost to the normal. A curious feature always noted in the condition is that remissions in the disease not infrequently take place of such character and unexpectedness that patients all but hopelessly lost take on renewed life and build up in every way to almost perfect health.

These remissions are frequently instigated by therapy, but it is a well-known fact that they may take place absolutely spontaneously and it is this fact more than any other that has given rise to a certain degree of scepticism regarding the benefits to be expected from splenectomy. It is fair to say, though, that while remissions in the disease are not at all common and may be spontaneous, after the occurrence of one or two or three of them, it is rare for another to come to pass. This has given rise to a general sentiment that if splenectomy offers some further chance to

patients who have already availed themselves of the hoped for remissions induced by therapeutic measures, it should be tried. This is about the position splenectomy occupies with regard to pernicious anæmia, at present.

Blood transfusion was used in pernicious anæmia almost as soon as it became possible to do it, but, as Crile remarked, the early cases were most unsatisfactory because of the ordeal of the operation and the feeling that little was to be gained by it, wherefore only those cases were submitted for transfusion which were practically moribund and which had previously undergone the usual remissions. However, a few cases were reported some years ago in which transfusion did help matters. In 1913, I read a paper before the American Medical Association entitled, "Therapeutic Possibilities of Transfusion," during the course of which I mentioned that encouraging results were being reported in pernicious anæmia, although I suggested that in this condition repeated transfusions seemed necessary, and I reported the case of a man admitted to the clinic of Dr. J. C. Bloodgood, who was transfused four different times from three donors and lived two years, after having been given up as lost. I furthermore said at this time that I believed that the "evidence against transfusion in this condition of obscure anæmia is based on too few cases

and that until the number is great enough to warrant accurate deductions, transfusions and repeated transfusions should be practised in every case in which they would seem to afford the slightest chance of success. By this I mean that the patient should be brought up for operation before he is moribund, before he is in such shape that anything short of a miracle could save him."

Shortly after this, with the improved methods of performing transfusion, more cases of pernicious anæmia, and some of them less advanced in their course, began to be submitted to the procedure with the result that it soon became fairly well recognized that new blood improved many patients quite markedly and started them on the road to a remission which often was quite prolonged. Curiously enough, transfusion was able to bring about a remission in a few cases where there had been one or two or three previously and where all subsequent efforts to improve matters had failed. But transfusion *per se* has never cured a case—at least not to my knowledge—so that it was only natural for splenectomy with its promised salvation to be warmly received.

At first, leaving out of consideration those few cases of ill-advised operation, the results seemed to justify all that was claimed—the down-and-out made recoveries in many instances little short of miraculous.

Cases in which there had been one and a half or two and a half millions of red cells prior to operation, a few months later boasted a count that was almost normal, even though the characteristic blood picture was still present under the microscope.

That this blood picture persisted was discouraging but in view of the improved health of the patients, it was felt that, even so, much had been gained. Many of the cases did not attain to a real or approximate normal count in point of numbers, although their physical improvement indicated normal blood findings. In fact, this has always been a remarkable feature of pernicious anæmia subjects; it has been astonishing to note how well many of them could get along with such low blood counts.

But the early enthusiasm for the operation was doomed to disappointment, because it was not long before cases which had done exceedingly well early after splenectomy began to relapse, and as more and more cases were done and time progressed, the relapses became more frequent, so that the need for a really comprehensive study of the whole subject became most pressing. This fortune supplied in the form of a paper read before the 1916 meeting of the American Medical Association in Detroit by Dr. Edward B. Krumbhaar of Philadelphia, from whose report I am making extensive references. Out of a total of 153 cases studied,

30 died within the first six weeks after operation, a mortality of 19.6 per cent. This of course was exceedingly high, and perhaps higher than it is at the present because, as I stated before, many cases were done at first, which a more careful consideration would have eliminated. Nor does it follow that in 20 per cent. of the cases some accident or unforeseen occurrence happened during the operation, but rather that the magnitude of the operation, together with the lowered vitality of many of the patients, resulted in thirty deaths out of 153 cases, within a period of six weeks after operation. The mortality at the present time, I would say, is hardly over 10 per cent. from any and all causes.

"Of the remaining 123 patients all but 24 showed a distinct improvement both in general condition and in blood picture. Of the twenty-four individuals that survived the operation, but failed to improve, a few were obviously harmed by it. The improvement noted in the majority of cases lasted varying periods. Thus at the end of six months, of the 53 patients who had survived operation for more than six weeks and were still under observation at that time, 44 had still continued to improve and none had died, but nine had already relapsed. At the end of the first year after operation, there remained 27 patients who were still under observation, of which number the initial im-

provement has been maintained in less than half—a rather discouraging showing when one takes into consideration the comparatively large number of cases under review."

Krumbhaar then goes on to say, "Estimation of the value of such a procedure as splenectomy in pernicious anæmia must take into consideration not only the actual results obtained, but a comparison, as far as possible, with the probable results if operation has not been undertaken. Thus, whereas we have seen that splenectomy caused a quick and marked improvement in 64 per cent. of all patients, natural remissions occurred at one time or another in 80 per cent. of the patients of Cabot's series treated by the older conservative methods. One cannot maintain from this that perhaps the improvement after splenectomy was only a coincidental remission, because the onset of improvement was too closely and constantly related to the post-operative period; but it does offer some basis for the contention that other methods of treatment may yield results as striking as those following splenectomy. However, from the aspect of the duration of the disease, the evidence is more in favor of the splenectomized series. In Cabot's series, almost half died in the first year of the disease, and of the remainder, one-third died in the next year. As the duration of the disease in the splenectomized series has

already averaged one and a half years before operation they should be more properly compared with the remainder of Cabot's group. By the end of the first year, conditions in the splenectomized group were as follows: Of thirty-three patients surviving the operation, twenty-four were still improved, three had failed to show improvement or had relapsed to their preoperative condition, and six had died. If post-operadeaths, however, were to be included, only about one-half of those whose fate was known were still alive at the end of the first year. From both these points of view, therefore, there are no clear indications as to the value of splenectomy."

Following splenectomy the blood changes were fairly constant, many cases had distinct post-operative blood crisis, following which the red cell count and the hæmoglobin began to rise and nucleated forms of cells began to disappear as the counts rose. The color index, however, remained high in nearly every case, and no matter how near normal the counts approached there was always the tendency to macrocytosis and poikilocytosis, so characteristic of pernicious anæmia. Those patients who succumbed early after operation showed little or no blood changes at all, except possibly a further destruction of red cells. Of all the cases reviewed by Krumbhaar, only five were living after two years, a most discouraging showing from certain

aspects, but if one chooses to take the view that all the cases were hopeless from the start, and that nearly all of those operated on had had one or two remissions prior to splenectomy, and were therefore doomed to a much earlier death, the evidence is not quite so bad.

One point worthy of careful thought has been noted by all of those who have had any experience with splenectomy in pernicious anæmia; namely, that the best results follow splenectomy in those cases that are not extremely anæmic at the time of operation and that have shown considerable fluctuations in the blood picture. Simply on a basis of common sense consideration, I came to this opinion early in the history of this procedure, and made an arbitrary rule that no patient should come to operation without a blood count of less than 2,000,000 red cells and a hæmoglobin of less than 30 per cent., and, acting on this determination, a series of cases done by Dr. J. M. T. Finney and myself have withstood operation remarkably well, with one exception, which will be mentioned later on.

Krumbhaar was able to secure information concerning the size of the spleen in 89 cases. In 28 cases (31 per cent.) the spleen was either small or approximately normal in size. In 41 cases (46 per cent.) the spleen was slightly enlarged and in 20 cases (23 per cent.) it was considerably enlarged. In other words, although seldom palpable before operation, it

was distinctly enlarged in over two-thirds of the cases. If the results of splenectomy are subdivided according to the size of the spleen, it will be seen that better post-operative results were obtained in the cases with enlarged spleens.

It is in this connection that I quote one case Dr. Finney and I had, which failed to show the slightest evidence of improvement after operation. The patient was a man forty-four years of age, married, travelling salesman. He had the usual progressive course of pernicious anæmia, and had finally come under our care with a red count of only 800,000 cells and a hæmoglobin of 18 per cent. His condition was so precarious that I immediately did a blood transfusion, in an effort to get him into shape for splenectomy. A few days later his red cell count was 1,400,000, hæmoglobin 32 per cent., but the blood destroying agencies in his circulation were so active that within a week his count had taken a decided fall, and, curiously enough, his spleen could not be felt nor even accurately located by percussion. Therefore, in an almost hopeless effort to save him, I started a second transfusion, during the course of which Dr. Finney removed a spleen that was barely half the normal size. Two days after operation his hæmoglobin was 24 per cent. and his red cells a little over 1,000,000, but he did not do well, was most uncomfortable and desperately weak, and within

a few days his hæmoglobin had dropped to 18 per cent.; the reds to 800,000 cells. I then did an unavailing third transfusion, the patient dying a few days later from a continuous decrease in the elements in his blood, thirty-four days after splenectomy. One notable feature of this case was that in spite of repeated search there was hardly a nucleated red cell to be seen either before or after splenectomy, thus indicating that at no time was there an attempt on the part of the patient's bone-marrow to produce new blood. This case illustrates in a striking manner the truth of statements made by Dr. Krumbhaar that those cases of pernicious anæmia having small spleens do not seem to do well under any form of therapy. This is the only case in our series of ten in which we have found a definitely small spleen, and it is the only one where at least temporary improvement has not followed the operation.

As for the further benefits of splenectomy, our own results agree with the majority that the cases are remarkably improved for the time but invariably relapse.[1] Sometimes they will improve under rest and arsenical treatment and, in addition to this, repeated transfusions seem to postpone the inevitable end; but as for permanent cure, we have nothing to report.

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[1] At the present writing I have just transfused for the second time one of these patients who had her first relapse just a little over one year after removal of her spleen.

Our most hopeful case is that of a woman who is now beginning her third year, but whose condition leaves much to be desired.[2] It is therefore evident that whatever the cause of the distinct improvement after splenectomy, simple removal of the spleen does not remove the cause of the disease. It seems rather that a major destroying force has been removed from the circulation without whose continual irritation the bone-marrow is able to produce blood-cells. It is conceivable that the relapse subsequent to splenectomy is due to hæmolymph-nodes, accessory spleens and even the liver taking over the functions of the spleen, although this has not been definitely proved.

Finally, it is proper to consider just what are the indications for splenectomy in pernicious anæmia. According to Krumbhaar, " One or two lines may be followed and it is as yet early to say which, if either, is correct. If splenectomy merely induces a remission, and this is at present the opinion of the majority of observers, it would be logical to undertake it only as a last resort, when all other measures have proved unavailing and only with the hope of prolonging life. Even under such limitations, however, the procedure has already proved its value, and in several cases

[2] This patient has just recently survived an operation for ruptured appendix with widespread peritonitis.

moribund patients have been brought back to a life of comparative well-being for many months. Assuming, on the other hand, that an occasional patient may be, for practical purposes, cured of the disease, and giving due weight to the view that greater and longer continued improvement is obtained if the operation is performed before the disease has reached its final stage, it would then be advisable to undertake it as soon as possible. Another factor that may prove to be decisive is whether or not increased hæmolysis can be proved. In those cases with clinically enlarged spleen, icteroid appearance, and increased urobilin output, without increased resistance of the erythrocytes, the prognosis is distinctly more favorable than in the opposite types. The condition of the bone-marrow is also important, splenectomy being contra-indicated if the bone-marrow is persistently aplastic. It has also been a matter of clinical observation that those individuals in whom spinal cord symptoms have already developed are less apt to be helped by the operation."

In summarizing this chapter on pernicious anæmia, I can perform no better service than by giving the conclusions reached by Dr. Krumbhaar *in toto,* since his study has been critical and fair-minded, and his findings have agreed so thoroughly with those reached independently by nearly everyone who has been engaged in the actual clinical study and treatment of

pernicious anæmia. These conclusions are as follows:

1. Of the 153 patients studied, 19.6 per cent. died within six weeks; a distinct improvement in the clinical condition and in the blood picture occurred in 64.7 per cent., and no improvement in 15.7 per cent.

2. The rather high post-operative mortality (practically 20 per cent.) may be due to poor choice of cases in the early series. As a much greater proportion of the more recent cases has survived the operation, the true post-operative mortality is probably much less than 20 per cent.

3. Of the individuals who showed improvement shortly after operation, nearly two-thirds of the total number, a large number have failed to maintain this improvement, or have since died in a relapse or from intercurrent disease.

4. Although a few have continued in good condition during the period of observation (over two years), in no case can it be said that a cure has been effected, and the blood of these individuals continues to show many of the characteristic signs of pernicious anæmia.

5. On account of the improvement that follows splenectomy, it would appear to be not only a justifiable, but in many cases an advisable, procedure; but in no case should a cure be promised or the operation undertaken except under the most favorable conditions.

6. The best results are obtained if the operation is preceded by one or more transfusions, and those patients who relapse after operation may still be greatly helped by transfusion. Whether or not transfusion would have produced equally good results in the absence of splenectomy is a question that cannot at present be decided.

7. The most favorable results may be expected in individuals who have not passed the fifth decade, in whom the disease has not progressed for more than a year, and who have a relatively good blood picture (that is, an anæmia that is not of too extreme a degree or of the steady, progressive type). Individuals with enlarged spleens have done better than those in whom the spleen was small or of normal size, as have also those suffering from an anæmia characterized by excessive hæmolysis.

8. The opposite of these conditions should be considered as unfavorable factors, as should also the existence of spinal cord symptoms or the presence of an aplastic bone-marrow.

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CHAPTER XI

TRANSFUSION FOR HÆMOPHILIA, MELÆNA NEONATORUM, PURPURA, JAUNDICE

No more interesting group of diseases is to be found than that of the so-called hemorrhagic diseases, nor is there a group which presents for solution a more intricate set of problems, since under this heading are to be found a number of different morbid conditions, having in common the one element of bleeding. The blood loss varies in location and severity from insignificant cutaneous hemorrhages in mild cases of purpura to appalling and even fatal hemorrhages in the more serious types of these affections.

According to Moss and Gelien, "An enumeration of the diseases in which hemorrhage is or may be associated, and which are sometimes designated hemorrhagic diseases includes:

" Hæmophilia, hereditary and spontaneous.

" Hemorrhagic diseases of the newborn, of which there are doubtless several forms.

" Purpuras, acute, chronic, simple, rheumatic, senile, etc.

" Jaundice.

" Grave anæmias.

"A heterogeneous group, including nephritis, typhoid and other severe infections."

It is unnecessary, for the purposes of this monograph, to enter upon a discussion concerning the etiology of these various conditions, especially since there is such profound obscurity and so many contradictions regarding them that it could not be profitable. Those interested are referred to special articles. But since hemorrhage is their common feature, and the one element that concerns us because of its danger, and since this bleeding is of spontaneous character and most refractory from every standpoint, we pause to note that a defect in the coagulation apparatus of the blood is considered to be present in each of the various conditions. This, of course, is the common-sense viewpoint, for how else could spontaneous bleeding occur? Opinions differ in regard to the element of coagulation lacking, and in regard to the cause of the deficiency whatever it may be, some inclining to the belief that it is an infection of an obscure order, others that it is a developmental deficiency in the make-up of the blood or tissue of those afflicted, perhaps of hereditary origin. Evidence is accumulating, however, which influences the belief that some forms are the result of infection, while others present developmental deficiencies of a serious order. Of this latter type, the most striking example is to be found in hæmophilia,

in which condition Howell has clearly demonstrated that the fault is to be found in a lack of prothrombin, one of the elements necessary to the coagulation of blood.[1] Thus it may very well come to pass that the various disease entities will be found to differ only in the radicle of the coagulation apparatus that is absent, though much work remains to be done before anything of a definite nature can be said.

Hæmophilia is perhaps the best known member of the group of hemorrhagic diseases because of its distressing character and its peculiarly deadly nature. Without question many so-called "bleeders" reach maturity, but it is doubtful if many of them live an ordinary span of life—the great majority die within the first few years or, surviving these, pass through numerous harrowing experiences, only to succumb in a culminating attack more terrible than any previous. Very possibly the conditions may be outgrown in a few instances, thus accounting for the fact that bleeders are rarely seen among those who have passed early adult life.

The pathogenesis of the condition remains obscure. According to Howell a deficient amount of prothrombin is found in the blood,[1] while Morawitz accounts for the bleeding by a lack of thrombokinase. Both

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[1] See Chapter I for Howell's theory of coagulation.

theories have their adherents, but the trend of opinion rather seems to favor Howell's view. According to Hess, " the plasma of the hæmophiliac has a delayed clotting time, varying generally from about one-half hour to many hours," which explains the prolonged intractable bleeding associated with the condition in cases of accidental wounds. It is well to note, though, that marked variations in coagulation time are quite frequently found in recognized cases of hæmophilia—especially after some previous hemorrhage, when, as first mentioned by Sahli, instead of the blood being delayed in its coagulation, a very rapid clotting may take place. No explanation has been forthcoming for this peculiar phenomenon.

Cellular examination of hæmophiliac blood reveals nothing unusual, even the platelet count, as shown by Duke, Hess and others, being normal. This latter finding, though, is of interest and aid in differentiating *hæmophilia* from *purpura,* where the platelet count is usually found quite low. Still another point in differentiating the two conditions is the so-called " bleeding-time," by which is meant the tendency to bleed from a puncture wound, such as is made by a hypodermic needle. The bleeding time is considered to be about normal in hæmophilia, but increased in purpura.

It is unnecessary to dwell at any length upon the clinical course of the condition, since it is quite familiar

to all medical men and even to a great proportion of the laity. The common story is that the patient has received a small cut or abrasion, usually of an insignificant nature, but in spite of the ordinary home remedies, bleeding has not ceased. Since the condition is generally of a hereditary character, it is possible in the vast majority of instances to obtain a characteristic history, although I have occasionally been confronted with the story that the case in hand was the first one ever noticed in the family. One can readily understand the importance of securing accurate knowledge on this subject, because of the necessity for instituting proper therapeutic measures. Not infrequently cases of protracted ooze are encountered where the condition is by no means one of hæmophilia, and the ordinary surgical measures, properly used, suffice, whereas, if a definite story of hæmophilia is obtained, not only must the aid of the usual surgical measures be invoked, but preparations should be made without delay for certain additional measures.

Briefly, the treatment of hæmophilia resolves itself into the following steps:

1. Reassuring of the patient and the patient's family if possible.
2. Absolute rest and quiet for the patient.
3. A snug bandage over the wound surface.
4. A few drops of fresh human tissue juice over

the wounded area, if ordinary surgical measures such as pressure, ligation of bleeding points, etc., will not stop the bleeding. If tissue cannot be secured a few drops of fresh human blood may be dropped on the surface, or preferable to blood, human serum may be used.

5. Thirty c.c. of human serum[2] may be injected subcutaneously, or fifteen c.c. of it may be given intravenously. In lieu of the fresh human serum, subcutaneous injection of fresh human blood may be used, or, if nothing from the human is obtainable, animal serum, such as horse serum or rabbit serum, may be used. The serum therapy of this and allied conditions has been advocated chiefly by Weil, whose reported results were quite good. Unfortunately, later observations by other workers along similar lines show that the efficacy of serum in checking the bleeding encountered in hæmophilia and the other members of the hemorrhagic group of diseases, has been regarded with a little too much optimism. The present view concerning the matter, and I think it is the common-sense view, is that at the initial stage of hæmophiliac or any other intractable bleeding, the aid of serum should be invoked. If a cessation comes about, all is well and good. If not, and all other measures have failed, it is wise to proceed without delay to the last resort which is

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[2] Calcium salts have been found practically worthless.

6. *Blood Transfusion.*—Normal human blood, of course, has all the requirements for normal coagulation, and since, as noted above, one of these requirements, namely, prothrombin, is lacking in the blood of hæmophiliacs, it is but natural to suppose that the intravenous introduction of whole blood will bring about at least a temporary coagulation. And so it does clinically. It has even been suggested since this is so, that every person known to be suffering from hæmophilia should be advised of his blood group, and that he should have the names and addresses of several individuals of that group, who would be available upon a moment's notice, and would be willing to supply him with serum or blood in case of need. So far as my experience with the condition goes, a very small amount of transfused blood will bring about an almost immediate cessation of the bleeding, but of course the dosage must depend to a great extent on the actual blood lost before the transfusion. For cases of tremendous blood-loss it is not sufficient to merely insure coagulation, but the consequent anæmia must be relieved. I sometimes feel that the adherents of the serum therapy allow their enthusiasm to overcome their saner judgment when, in the face of continuous bleeding, they persist in giving repeated doses of serum. If two or three doses of serum fail to give results after a reasonable period, it is unlikely that larger quantities will achieve any

better results, so preparations for transfusion should be made and intravenous blood given without delay. In this way not only will many lives be saved, but the dose of blood required will be hardly over 100 or 200 c.c.

Not many months ago, late at night, I saw a little baby who had been circumcised six hours before. Previous to my arrival two attempts had been made to stop the ooze by suturing, but without success. The child was in very good condition, so I tried to stop it by placing additional sutures, also unavailing. The story was that an older brother had suffered a very severe hemorrhage after circumcision but had recovered. A sister, born one year before, had bled to death from an obscure form of vaginal bleeding. The father and mother were healthy, rather intelligent people, but had never even heard of anything like hæmophilia. The case seemed reasonably clear cut to me, so I immediately administered to the child 55 c.c. of citrated blood from its father. The bleeding ceased immediately, and the child made an uneventful recovery. In this case no serum was given. It was considered, but since transfusion is simple and is surer in its results than serum, and since the child was in the hospital, I felt that transfusion was the preferable measure.

Very recently, Dr. William H. Howell, of the Johns Hopkins University, has produced a substance known as *Kephalin,* which is made of brain tissue of the hog. It was his idea to secure an extract of that

tissue most active in stimulating blood coagulation, and since his experiments showed that the highly cellular brain was richest in activating properties, its tissue was chosen. Kephalin, which is now on the market,[3] can be obtained in any desired quantity, is especially efficacious if it can be applied directly to the bleeding point, and held in place either by bandage or other means. Not only is it of service in hæmophilia, but quite recently Dr. H. L. Cecil, of the Brady Clinic, reported most satisfactory results after its use in certain of the operations done in the Genito-Urinary Department of the Johns Hopkins Hospital. The method of procedure there is to use kephalin impregnated gauze for packing purposes or to make an ether solution of kephalin, dip sound or catheter into it, and allow this to remain in place over a wound area such as follows the " punch " operation for prostatic obstruction.

Dr. Howell himself has been able to stop subcutaneous bleeding in several cases of hæmophilia by feeding kephalin, but further trial must be made before definite results can be claimed for this method. However, with serum therapy, fresh tissue, kephalin, and finally blood transfusion, the fortune of those afflicted with hæmophilia seems at least a little rosier than it did a few years ago.

[3] It is made by Hynson, Westcott & Dunning, of Baltimore, also by Armour, of Chicago.

Melæna Neonatorum.—This term is applied to those instances of hemorrhage in the new-born, where shortly after birth—at times within twenty-four or thirty-six hours, earlier or later, spontaneous bleeding arises of an unknown origin. It usually comes from some part of the alimentary tract and is manifested by bloody stools, though at times it may come from the umbilicus or appear in the form of widespread subcutaneous hemorrhages while, in rarer instances, a combination may be present. The bleeding is always most dangerous because of its intractability and because of the fact that the subjects have so little blood to lose. The parents of these infants are practically always perfectly normal in every respect, and the delivery apparently has nothing at all to do with the condition, which may occur—in fact usually does—in one child and not in its brothers and sisters. Syphilis is supposed to be the cause in some cases, especially in those associated with bleeding from the umbilicus, and an obscure form of general infection is believed to be responsible for the remainder, an opinion unsustained by proof.

The mortality approaches 100 per cent. in untreated cases, and all cases may be said to have been untreated, so far as practical results were concerned, until Carrel of the Rockefeller Institute carried out a successful blood transfusion in the case of an infant

exsanguinated from this condition. This was in 1908 and the case, reported by Dr. S. W. Lambert, marks an epoch of the most startling character in the annals of blood transfusion, for since that time hundreds of patients suffering from this and allied conditions have been saved by means of transfusion, while previously all, or practically all, had been lost.

Until recently little babies have offered a most formidable problem in transfusion because of inherent difficulties encountered in working with them, so that great enthusiasm prevailed when Welch reported that he had cured 12 cases of melæna neonatorum by subcutaneous injections of fresh human serum, his average dose being 80 c.c. in 10-c.c. doses extending over a period of four days, but in exceptional cases 209 c.c. in five days. When Schloss in the following year reported that whole blood injected subcutaneously could be used in place of serum, which at times might be difficult to secure or at least would necessitate a delay, the difficulty was thought to be overcome.

As in the case of so many other forms of therapy, early reports were a bit exaggerated and subsequent investigations necessitated a certain amount of qualification in the claims of subcutaneous serum and blood. They do most certainly stop the bleeding in many of the cases but they do not succeed in a considerable proportion, for some unexplained reason. So that, as

matters now stand, it is advisable to give a subcutaneous injection of 15 or 20 c.c., or 30 or 40 c.c. of whole blood at the inception of every case of bleeding in the new-born, and if the desired cessation does not appear within an hour, or two, to resort to transfusion of blood without delay, the amount of blood transfused being anywhere from 35 to 90 c.c. or even 125 c.c. where there is severe exsanguination.

A case in point is one I did in January, 1916. A baby thirty-six hours old, delivery perfectly normal, suddenly began to pass blood from the bowel, and four hours later was given 15 c.c. of human serum subcutaneously. In spite of this, it continued to have bloody stools, and a few hours later showed signs of collapse, whereupon I injected 45 c.c. of blood into its internal jugular vein, its father serving as donor. Bleeding ceased immediately and the child made a perfect recovery.

The efficacy of transfusion in this condition became apparent before indirect transfusion was available as a practical method and one can imagine what a difficult matter it was to unite by means of a cannula an adult's radial artery to a twenty-four or thirty-six hour old infant's femoral vein, or even its external jugular vein, as was suggested by Beth Vincent. In fact, it was an all-night struggle in just such a case—the result of which was fortunately successful—that gave me the

idea of the two-piece transfusion tube that I devised in 1910. This simplified matters a good deal, but the needle and syringe method of Lindeman came along shortly afterwards and solved most of the difficulties. Even this offered problems, because a vein had to be isolated, and veins of infants are neither easy to isolate nor satisfactory to work with after preparation because of their delicacy and smallness. The whole matter was then settled by Helmholtz of Chicago, who showed that blood might be injected into the longitudinal sinus of these infants with great ease and without danger. It seems therefore that since serum will stop the bleeding in only a certain percentage of the cases and transfusion in practically all, the latter form of therapy, which is so simple to perform that it is hardly more complicated than a subcutaneous injection of whole blood or serum should be the method of choice.[4]

To summarize, then, *melæna neonatorum* is an obscure form of intestinal bleeding in the new-born which is always dangerous. It is the one member of the so-called hemorrhagic group of diseases which is known to be *cured,* once cessation of the bleeding is attained. Subcutaneous injection of serum will cause

[4] I think, however, that extreme care should be exerted in this procedure because of the ease with which the sinus wall could be punctured.

cessation in a certain proportion of cases, subcutaneous injection of whole blood will cause a cessation perhaps in a smaller proportion, while transfusion of blood will stop the bleeding in practically every case if carried out early enough. It is permissible to try serum or subcutaneous blood at the beginning of all cases of bleeding, but where prompt cessation does not follow, transfusion should be performed without delay. Where the bleeding has continued without treatment for any length of time, simple control is not sufficient, since the blood loss should be made up by transfusion. Finally, in view of the recent simple method of injecting blood into the longitudinal sinus as suggested by Helmholtz, it seems wise to transfuse every case as soon as it starts, rather than run the risk of failing to control the bleeding by the use of serum.

Purpura.—By this term is understood those bleedings of spontaneous and obscure origin that occur into the tissues. They may be subcutaneous, into the joints, into the deeper tissues, or the bleeding may become manifest by an intestinal seepage of a most intractable character. It is usually considered that purpura is due to some bacterial, metabolic, or chemical toxæmia, and for each theory certain substantiation has been found, such, for instance, as the subcutaneous hemorrhages encountered in the recognized septicæmias in support of the bacterial theory. But,

withal, the etiology is as obscure and unsatisfactory as is the therapy, and we are confronted with a dangerous recurrent disease which arises spontaneously, and occasionally, though not often, disappears spontaneously—and most mysterious of all, repeated examinations by many different investigators have yet to reveal the slightest abnormality in the blood picture except a diminuition or total absence of platelets as noted by Duke, and confirmed by later investigators.

Platelets are supposed to have a fundamental influence on blood coagulation and their absence from the blood might well account for the subcutaneous hemorrhages and the long continued bleedings encountered in purpuric conditions. But what causes the platelets to be absent and are they destroyed after being formed or are they never made in this condition? Purpuric spots and bleedings are but symptoms of an underlying condition, and an absence of platelets only explains the occurrence of the symptoms. By no means does this feature shed light on the etiology.

As a result some men consider the basic condition to be due to an inherent defect in the blood-vessel wall which under certain conditions, unexplained thus far, permits the blood to escape from its confines into the surrounding tissues in the form of the so-called purpuric spots. A fanciful explanation, perhaps, but one held by such a well-known investigator as Sahli of Switzerland.

Whatever the underlying cause, the condition is always to be regarded with concern because of the possibilities for trouble. Encountered in people of all ages, most cases are mild and yield to rest, diet, and the usual forms of therapy used for conditions of supposedly disturbed metabolism, while those cases which occur during the course of a recognized disease or infection, usually vary in intensity according to the improvement or progress of the primary condition. A certain number, though usually unassociated with any other demonstrable disorder, prove most resistant to all forms of therapy and proceed from bad to worse. I encountered such a case in 1913, the patient being a man of thirty, patient of Dr. Richard Bell of Staunton, Va., previously well, who first suffered with nose bleeds, then with subcutaneous hemorrhages all over his body, bleeding from his gums, and finally with intestinal hemorrhages of an exsanguinating variety. Horse serum, calcium, styptics of all varieties, and all other known methods of controlling bleeding were resorted to without avail until his condition became so desperate that a blood transfusion was necessary to save his life. A more shocking sight I have never seen than that poor fellow—drops of pale, thin blood were oozing from his nose and gums to such extent that he was able to articulate only between expectorations of mouthfuls of blood, and his entire skin was

peppered with purplish-blue spots of subcutaneous hemorrhages of all shapes and sizes. The transfusion stopped the bleeding immediately; even before its conclusion, the oral and nasal ooze had ceased, and his condition progressively improved to such extent that he was able to leave his bed and seemed on the road to recovery. Some months later he died in a recurrence.

I have knowledge of another stubborn case, that of a young woman, who every once in a while has subcutaneous hemorrhages scattered over her body and very frequently has abdominal symptoms of a most obscure character, which are probably nothing more than intestinal manifestations of the same condition. Her blood has been most painstakingly investigated by Dr. Howell and Dr. Moss with negative findings. In perfect health at present, she nevertheless has at the present writing a large purpuric spot just to one side of her soft palate which made its appearance just the other day and is a single manifestation.

Many transfusions have been done for the condition; Peterson of New York reports 12 transfusions in 7 cases, 3 of which ceased to bleed and recovered for the time being, while 2 died. The other 2 relapsed within a period of a year. This is the usual story.

I have under my care now a young girl of nineteen, who has a history of bleeding from the uterus

extending over a period of eight years. Repeatedly exsanguinated, always more or less in trouble, she was transfused about one year ago with temporary benefit. When the bleeding recurred she was treated with radium by Drs. Kelly and Burnam, and the uterine bleeding ceased. A few months ago intestinal bleeding became the order of the day, and her condition progressed steadily downwards until she travelled from her home in St. Louis to Baltimore with the hope that radium would again prove beneficial. On her arrival, however, she was so anæmic and weakened that a hurried transfusion was necessary to save her life in this emergency; but before resorting to transfusion it was noticed that, in addition to her active intestinal bleeding, numerous large purpuric spots were scattered all over her body. After twelve transfusions and a cecostomy for purposes of irrigation this patient was sent home looking the picture of health, all bleeding stopped and with a blood count almost normal. The most striking feature of the case was an almost total absence of platelets. Even when the patient's blood approached the normal count but little increase was to be noted in their number, though late reports from the family physician tell of a slow but steadily increasing platelet count as time wears on.

Further citation of cases, with which the literature abounds, is superfluous. In purpura we are dealing with a dangerous obscure form of bleeding which

yields to no form of therapy so far as a cure is concerned, but which occasionally recovers spontaneously. Most cases are mild, but many are desperate in the extreme; even so, temporary recoveries and long remissions may be expected in certain of the worst. Subcutaneous injections of serum arrest the bleeding in some cases, intramuscular injections of whole blood stop it in others, blood transfusions apparently arrest it in a great many more. Nothing will effect a permanent cure so far as is known.

Jaundice.—Bleeding in icteric conditions is quite common and always dangerous, yet there is great confusion regarding the true nature of the phenomenon. The cause of this uncertainty is probably due to the fact that, although the type of bleeding is the same in all forms—being an intractable ooze from all mucous membranes—the blood condition differs according as the jaundice is of the obstructive type or of the non-obstructive type. In the first variety there is no disease of the liver, while in the second there is, although it is well to remember that considerable difficulty arises from a clinical inability to determine which cases will bleed and which will not. It might be thought, *a priori,* that the deeper the jaundice the more likelihood of bleeding following operation; this may be true to a certain degree, but it cannot be taken as a guiding rule. Many of the most deeply jaundiced patients come through their illness without a

sign of bleeding while others far less jaundiced come to grief.

In many clinics the custom has arisen, as a consequence, of giving all jaundiced patients 15 grains or more of calcium lactate as a prophylactic three times a day for several days prior to and following operation, but opinions differ as to the efficacy of the treatment in preventing hemorrhage. The trouble is that the prophylaxis has not been carried out rigidly enough to really tell whether it does or does not help. Prevention is most urgent, however, since once the bleeding has started it is always to be feared. Calcium lactate practically never stops it, and the various sera are of little more service, although isolated cases are to be found in the literature where a favorable outcome did follow their injection. Of the three—rabbit, horse and human serum—the human variety is to be preferred, but transfusion of whole blood seems to be of more service than any one or all three put together.

It should be noted, though, that the two conditions may be associated. Where the jaundice is purely of the obstructive type, the delay in blood coagulation has been shown to be due to a lack of available calcium in the blood caused probably by an unusual binding of the calcium normally present by the bile pigments (Whipple) which thus renders it useless for coagula-

tion purposes. To meet this condition it has been found possible to administer calcium by mouth, although its absorption from the intestinal tract is so slow that it must be administered over a period of several days before any marked effect on the coagulation tissue is seen. Calcium lactate is usually employed in 100-grain doses a day. Intravenous injection is probably practicable but has not been extensively used, chiefly on account of the insolubility of the drug.

In the bleeding associated with liver changes, there is rather conclusive evidence to show that the prothrombin-antithrombin[5] balance, always of necessity a most delicate one, has been upset by the excessive production of antithrombin by the liver. As a consequence the entire mechanism of blood coagulation is thrown out of gear with the resultant well-known intractable fatal hemorrhages. And since the fault here has nothing to do with calcium of the blood, it is evident that calcium administration is useless, a more logical procedure being the administration of something containing sufficient prothrombin to bind the excessive antithrombin and thus bring about the normal conditions necessary for blood coagulation. The blood of a normal individual, of course, contains the desired element, and it has been found that transfusion of fresh whole blood brings about the equilibrium

[5] See Howell's theory of coagulation, Chapter I.

that results in coagulation and cessation of bleeding, although it obviously can have no effect on the underlying condition of the liver. So that while transfusion is of definite service in the non-obstructive icteric conditions it must be clearly understood that nothing of a permanent nature can be expected unless the hepatic condition can be rectified.

In the obstructive type of jaundice, even transfusion fails to stop the bleeding in all cases and in numerous instances the hemorrhage has continued to a fatal ending. It is only fair to say, however, that most of the fatal cases have been pretty far advanced when blood was transfused, this procedure being held as a last resort in these patients for whom calcium is usually started as soon as the slightest bleeding takes place; if it continues more calcium is given, and if this does not stop it the aid of serum is invoked, whereas early transfusion would probably save almost every one of them.

In concluding this chapter it may be said that any of the hemorrhagic group of diseases is to be feared at all times, because of inherent possibilities for danger. Based upon an obscurely deranged coagulation mechanism that is different in each unit of the group, diagnosis, as a rule, is not specially difficult but therapy is rather unsatisfactory, chiefly, perhaps, because of the obscurity of etiology. The type known as melæna

neonatorum is the only one which can apparently be cured by anything that will stop the bleeding, of which agents transfusion of blood is by all means the surest. In the remaining types the basic condition is apparently unchanged by any form of therapy, but in all of them the bleeding can usually be stopped, either by serum injections or preferably by blood transfusion, by which means remissions of greater or lesser duration may be secured. These alleviations are most desirable not only because they prolong life, but because the conditions, themselves of either hereditary or spontaneous origin, occasionally vanish in a wholly unaccountable manner.

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CHAPTER XII

LEUKÆMIA. SPLENIC ANÆMIA (BANTI'S DISEASE). CERTAIN TOXÆMIAS

From the standpoint of blood transfusion, the leukæmias are most discouraging, chiefly because many cases exhibit such a pronounced change for the better immediately following the blood introduction—only to be followed by a reversion to the pre-transfusion state in an equally short period. In other conditions, if any improvement occurs at all, it is customary for it to last at least a reasonable period—the remissions seen in pernicious anæmia are an example—but the basic cause of leukæmia is evidently an agent of such markedly different character that any inhibition of its activities that may be caused by blood transfusion is only a temporary phase in a steadily progressing disease that always ends fatally.

A case in point is that of a little boy twenty-one months old, the patient of Dr. John Ruhräh, who became ill in November of 1914 and on examination was found to be suffering from acute lymphatic leukæmia of such grave degree that his course was one of rapid progress down hill, in spite of all supportive treatment. An indirect transfusion of 90 c.c. of blood was followed by a prompt drop in temperature, a definite fall in his white cell count with a change for

the better in the differential count, and, best of all, a rise in his red cells and hæmoglobin. The child's physical condition improved correspondingly, he began to relish his food, he lost his waxy look, was able to be up and about, and had even been taken out for a walk by his nurse when he suddenly relapsed—only three or four weeks after the beginning of his remission. From that time on his downward course was even more rapid, and a second transfusion was utterly unavailing. He died just seven weeks after the first introduction of blood.

A case almost identical with this occurred in a man of forty-eight years, a patient of Dr. W. T. Willey, who had undergone without improvement a course of X-ray treatments prior to my seeing him. His count before transfusion was red blood-cells, 1,360,000; white blood-cells, 356,000 (98 per cent. lymphocytes); hæmoglobin, 20 per cent. Two and a half weeks later, after his second transfusion, his count was red blood-cells, 1,840,000; white blood-cells, 108,000; hæmoglobin, 32 per cent., showing a marked diminution in the number of his white cells, although differentially they were still largely composed of lymphocytes. His physical condition was very much better [1] during this

[1] Blood transfusion has been used in leukæmia not with any idea of effecting a cure but rather in the hope that the condition might be influenced to take on a chronic form, with a resultant prolongation of life.

time and it began to look as if some real benefit might come about, when an unaccountable enlargement of the glands in the left side of the neck became apparent. From that time on, the patient rapidly lost ground. His white cells became as numerous as ever, he was unable to build any red cells, his hæmoglobin fell, and he began to have slight bleedings from the gums, and irritating ulcers of the tongue. A third transfusion was performed but was unavailing, the patient dying of a terminal pneumonia a short time later.

I have had a few other cases of this kind; they have all gone the same way, and others have had similar corroborative experiences. It may therefore be concluded that transfusion can offer little or no hope in the condition. Just why the introduction of fresh blood causes even a temporary halt in the disease I am at a loss to say, and how it destroys the white cells is equally obscure. Perhaps there is no destruction, for it is conceivable that the lowered white cell count may be due to blood dilution consequent upon increased blood bulk or a diminished output of white cells. Whatever the cause, the new blood is of little sustaining power since the old régime soon recommences, apparently possessed of even increased vigor.

Splenic anæmia or, as it is called in its later stages, *Banti's disease,* is apparently cured by removal of the spleen, and is concerned with transfusion only when the

anæmia becomes so pronounced that new blood is desired in order to decrease the operative risk. Transfusion alone will favorably influence the anæmia, but since splenectomy has proved to be of such undoubted value, simple transfusion is not to be considered as adequate treatment.

A most instructive case in point was that of a little boy of eight, a patient of Dr. W. S. Thayer, who had had splenic anæmia for several years until finally no hope remained for him but removal of the spleen. His blood picture was so low that a preliminary transfusion was done the day before operation, but a few hours later the boy vomited practically every drop of blood given him, probably from a ruptured œsophageal or gastric varix. Next morning he was transfused again, and during the actual course of the blood transfusion his spleen was removed by Dr. J. M. T. Finney. A gradual but quite satisfactory recovery ensued, and he left the hospital in good condition, only to die several months later from another gastric hemorrhage.

In certain forms of toxæmia and certain poisons, blood transfusion has seemed to be of value, but the number of cases reported is so limited, that little of an authentic nature can really be said and I merely mention the possible agency of transfusion in these conditions for the sake of completeness.

A few transfusions have been carried out in eclampsia and the toxæmia of pregnancy. In the latter condition, Keator reports a successful case, and one of my own seemed about to have a successful outcome when an unexpected heart collapse thirty-six hours after transfusion ended matters. In neither eclampsia nor toxæmia of pregnancy would I think of advocating blood transfusion as a cure, since in general the proper obstetrical measures bring about relief, but it seems worthy of a more extended trial in those fulminating cases where obstetrical resources have proved unavailing and a fatal ending appears imminent. Preliminary bleeding probably should be carried out prior to the introduction of the fresh blood in order to eliminate as much toxic matter as possible.

Of the poisons, illuminating gas has been shown to yield best to the introduction of new blood, but the pulmotor as used by the various gas companies seems to give as good results as can be expected in the majority of cases. I have never done a transfusion for the relief of this condition, and few are found in the literature, although it has been the subject of a considerable amount of experimental work.

A most brilliant result followed transfusion in a case of benzol poisoning treated in the Johns Hopkins Hospital in 1914. Repeated transfusions were carried out by Dr. R. D. McClure, who reported

the case before the 1916 meeting of the American Medical Association. So far as I am aware, it is the only case of the kind on record, due probably to the fact that benzol poisoning is so rarely encountered.

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APPENDIX

CONTAINING HÆMOLYTIC AND AGGLUTINATION TESTS THAT ARE TO BE CARRIED OUT PRELIMINARY TO EVERY BLOOD TRANSFUSION EXCEPT THOSE OF THE MOST URGENT CHARACTER. THE TESTS GIVEN ARE AS FOLLOWS: (1) MOSS' METHOD OF GROUP TESTING; (2) BREM'S SIMPLIFICATION OF MOSS' GROUP METHOD; (3) SIMON'S METHOD OF TESTING OUT DONORS DIRECTLY AGAINST THE RECIPIENTS; (4) SYDENSTRICKER'S METHOD OF TESTING OUT DONORS DIRECTLY AGAINST THE RECIPIENT.

MOSS' METHOD OF GROUPING BLOODS FOR TRANSFUSION.

ACCORDING to Moss,[1] whose article on Isoagglutinins and Isohemolysins, written in 1910, still remains an undimmed landmark, all individuals can be divided into four groups as regards their blood according to the ability of their serum to agglutinate the corpuscles of other individuals, and according to the ability of their corpuscles to be agglutinated by the serum of other individuals.

[1] W. L. Moss, "Studies on Isoagglutinins and Isohemolysins." Bulletin of the Johns Hopkins Hospital, vol. xxi, No. 228, March, 1910, pp. 63–70.

These groups which were based originally on 1600 tests, have been borne out by thousands of subsequent tests by numbers of observers and are as follows:

Group I (10 per cent.): Sera agglutinate no corpuscles. Corpuscles agglutinated by sera of Groups II, III and IV.

Group II (40 per cent.): Sera agglutinate corpuscles of Groups I and III. Corpuscles agglutinated by sera of Groups III and IV.

Group III (7 per cent.): Sera agglutinate corpuscles of Groups I and II. Corpuscles agglutinated by sera of Groups II, IV.

Group IV (43 per cent.): Sera agglutinate corpuscles of Groups I, II and IV. Corpuscles agglutinated by no serum.

The details of the test are as follows:

"The technic employed in all of the tests here reported was carried out with surgical asepsis, and great care was taken that the syringe, pipettes, test-tubes, and all glassware used were not only sterile but very clean. Blood is taken from a vein at the elbow. For this purpose the skin over the vein is rendered aseptic and about 20 c.c. of blood is withdrawn by means of a syringe which previously has been boiled and then washed out with a solution containing 1.5 per cent. sodium citrate and 0.85 sodium chloride; this removes any water which remains in the syringe after boiling and which might cause slight laking of the blood. Two sterile centrifuge tubes are ready to receive the blood

as soon as it is withdrawn, one being empty and the other containing 10 or 12 c.c. of 1.5 per cent. sodium citrate in 0.85 per cent. sodium chloride solution. Into the tube containing the sodium citrate, 3 c.c. of blood is introduced for corpuscles, and the remaining blood is put into the other tube for serum. The corpuscles are further prepared by centrifugalizing them out of the sodium citrate solution, pipetting off the supernatant fluid and washing them twice with 0.85 per cent. sodium chloride solution to free the cells from serum. After the last centrifugalization, which is continued until the cells are thoroughly sedimented, the supernatant fluid is pipetted off and 0.5 c.c. of the corpuscles is transferred to 9.5 c.c. of 0.85 per cent. sodium chloride solution, thus making a 5 per cent. suspension.

"The tube containing the blood of the serum is allowed to clot and after about half an hour the clot is carefully separated from the sides of the tube with a sterile platinum needle, after which the serum is easily obtained by a few minutes' centrifugalization. The clear serum is then pipetted off from the clot and transferred to another tube. Serum and corpuscles are similarly obtained from a number of individuals.

"The further procedure consists in combining equal quantities (usually 0.25 or 0.5 c.c.) of serum and suspension of the corpuscles so that the action of

each serum is tested on the corpuscles of every member of the series separately. These mixtures having been made, the tubes are shaken to distribute the corpuscles evenly through the serum, and are then allowed to stand in the thermostat at 37.5° C. for two hours, after which they are placed in the icechest over night. Readings are made at the end of the two hours in the thermostat and after the tubes have stood over night in the icechest. Agglutination and hæmolysis are easily determined by the naked eye, and the results of the reading at the end of two hours in the thermostat and after having stood over night in the icechest differ, if at all, only slightly in amount.

"Before examining the results obtained, it may be stated that no constant differences were found between the agglutinating or hæmolysing abilities of sera in health and in disease. The serum of a healthy individual might agglutinate or hæmolyse the corpuscles of some healthy individuals, but fail to agglutinate or hæmolyse those of other healthy individuals and the same variations were noted in its action on the corpuscles of patients suffering from a variety of diseases. The same relations were found to exist between the serum in disease and the corpuscles of diseased and healthy individuals. . . .

"In regard to the relationship existing between isoagglutinins and isohæmolysins, I may say that ag-

glutination frequently occurs independently of hæmolysis, but that the inverse relation occurs, *i.e.*, hæmolysis without the simultaneous or preceding occurrence of agglutination seems less likely. In my first experiments hæmolysis without agglutination was frequently recorded, but closer attention to this point in subsequent experiments led me to doubt the correctness of earlier observations.

"Agglutination is a phenomenon which concerns the corpuscle as a whole, while hæmolysis is a phenomenon which destroys the integrity of the corpuscle, and it is possible that agglutination cannot persist among corpuscles which have been damaged by the action of hæmolysins. As a rule, however, agglutination proceeds more rapidly than does hæmolysis and by observing the action of a serum, which contains both agglutinin and hæmolysin, on susceptible corpuscles, one frequently sees agglutination set in which is subsequently broken up as hæmolysis takes place; so that if the observations are not made until the lapse of two hours, in a case where the hæmolysin is not quite sufficient to dissolve completely all of the corpuscles present, we may get the appearance of hæmolysis having taken place without agglutination."

Certain of Moss' conclusions that might be helpful are as follows:

"I. Isoagglutinins occur in the serum of about 90 per cent., and isohæmolysins in about 25 per cent. of adult human beings.

"II. These bodies appear with approximately the same relative frequency in health and in various diseases and therefore have no diagnostic significance.

"III. Human beings can be divided into four groups according to the ability of their serum to cause isoagglutination and of their corpuscles to be isoagglutinated.

"IV. The serum of members of any one group will not agglutinate or hæmolyse the corpuscles of other members of the same group but will agglutinate and may hæmolyse the corpuscles of members of any other group except those of Group IV. This may have a practical application in the transfusion of blood from one individual to another.

"V. Isoagglutination may occur independently of isohæmolysis but isohæmolysis is probably always preceded or accompanied by isoagglutination."

BREM'S METHOD OF GROUP TESTING

Moss's method of grouping bloods has been somewhat simplified by numerous investigators, all such short-cuts having for their basis one or two known bloods. Probably the best known is that of Walter V. Brem.[2] the technic of which is as follows:

"Let II represent a known blood belonging to Group 2, and X a blood the group of which must be determined. Five or six drops of II blood are collected in a small clean dry test tube or centrifuge tube, and 1 or 2 drops, according to the size of the drops, in another tube containing 1 c.c. of 1.5 per cent. sodium citrate in 0.9 per cent. salt solution, which gives one approximately a 5 per cent. suspension of corpuscles. The percentage does not have to be exact. The X blood is collected in the same way in two similar tubes. The bloods in the dry tubes are allowed to coagulate, the coagulum is loosened from the side of the tube with a platinum wire, and the tubes centrifugalized to separate the serum. Serum and corpuscles are now ready for the tests. Platinum loopfuls of serum and corpuscles are placed on coverslips, which are inverted over an ordinary cell slide rimmed with petrolatum. Two loopfuls of serum are used and one of corpuscle suspension. The slides are gently rolled from side to side to agitate the corpuscles in order to bring them into contact with each other. Agglutination, if it occurs, takes place at room temperature within five minutes. It can usually be detected with the naked eye, showing as brick red particles, but

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[2] Walter V. Brem, "Blood Transfusion with Special Reference to Group Tests," (J. A. M. A., July 15, 1916, vol. No. 3, p. 190.)

should be examined, also, with the low power objective of the microscope. Rouleaux formation of red corpuscles must be differentiated from small clumps due to agglutination."

ILLUSTRATIONS OF GROUP DETERMINATIONS (THE FIGURES REFER TO LOOPFULS)

2 II serum + 1 x corpuscles = agglutination
2 x serum + 1 II corpuscles = 0

Group 2 serum agglutinates the corpuscles of Group 1 and 3 only. But Group 3 serum agglutinates the corpuscles of Group 2, which does not happen in the foregoing test with X serum and II corpuscles. The X blood does not belong, therefore, to Group 3, but must belong to Group 1.

2 II serum + 1 x corpuscles = agglutination
2 x serum + 1 II corpuscles = agglutination

Each serum agglutinates the other corpuscles, so the two bloods belong to the reciprocal Groups 2 and 3, that is, the X blood belongs to Group 3.

2 II serum + 1 x corpuscles = 0
2 x serum + 1 II corpuscles = agglutination

Group 2 serum does not agglutinate Group 2 or Group 4 corpuscles, while it does agglutinate the corpuscles of Groups 1 and 3. The X blood belongs, therefore, to Group 2 or Group 4. Which one is determined by testing X serum against II corpuscles, which it agglutinates. A serum does not agglutinate

corpuscles belonging to its own group, so the X blood does not belong to Group 2, but must belong to Group 4, the serum of which does agglutinate Group 2 corpuscles.

2 II serum + 1 x corpuscles =	0
2 x serum + 1 II corpuscles =	0

The X blood belongs to the same group as the blood used for testing, Group 2.

According to Brem, this method of determining the group of an unknown blood requires not more than fifteen minutes after the bloods are obtained, and only small quantities of blood such as can be obtained from a puncture of the finger tip, are necessary.[3]

TEST FOR AGGLUTINATION AND HÆMOLYSIS AS CARRIED OUT BY DR. CHARLES E. SIMON OF THE UNIVERSITY OF MARYLAND.

By many men it is considered quite unnecessary to carry out the group method of testing, a more direct means of attaining the same end being that of testing all prospective donors directly against the recipient until a suitable donor is secured. Such a test is as follows:

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[3] A most excellent article on the subject of Agglutination and Hæmolysis is that by Minot. It is comprehensive, gives numerous tests, and contains a carefully selected list of references. See Minot, George R.: "Methods for Testing Donors for Transfusion of Blood and Consideration of Factors Influencing Agglutination and Hæmolysis." *The Boston Medical and Surgical Journal*, May 11, 1916, p. 667.

1. *Preparation of Serum and Blood-cell Suspensions.*—A few drops of blood from each of the donors and from the recipient are collected in small dry glass test tubes. A few drops from each donor and the recipient are also placed in tubes containing about five cubic centimeters of a 1.5 per cent. solution of sodium citrate in physiological salt solution. *Each tube is marked carefully for identification as soon as obtained.*

The undiluted specimens of blood are centrifugalized, the sera pipetted off (each serum with its individual pipette) and transferred to correspondingly labeled dry test tubes. The specimens collected in citrate are centrifugalized, the supernatant fluid pipetted off (each with its individual pipette) and discarded, and the cells remaining washed a couple of times with saline solution. Very thin and homogeneous normal saline suspensions of each specimen of washed cells are finally prepared.

2. *Preparation of Mixture of Donor's Cells and Recipient's Serum and vice versa.*—A series of glass slides (as many slides as there are prospective donors), is prepared as follows: On one side of each slide two small rings of vaseline are made, one toward either end. The inside diameter of these rings should be about 1 to 1.5 centimeters. The slides are labeled so as to correspond with the identification mark of each donor. Each slide thus has two vaseline " chambers "

and represents one donor. The right hand chambers are marked " S " (serum) and the left hand chambers " C " (corpuscles).

Into each " S " chamber is placed a drop of serum from the corresponding donor, while into each " C " chamber is placed a drop of the blood cell suspension from the corresponding donor. To all of the " S " chambers is then added a drop of the washed cell suspension of the recipient, and to all the " C " chambers a drop of the recipient's serum. The contents of each chamber are thoroughly mixed. Each chamber is then sealed by carefully superimposing glass coverslips over the vaseline rings. With a little dexterity the sealing can be effected so as to spread out the contents of each chamber into a very thin layer between the slide and the cover slip. The specimens are now placed in the thermostat at 37° C., and observed for agglutination and hæmolysis at the end of one hour, and again after a second hour. In cases of emergency, it may be necessary to shorten the incubation period to one-half hour, but two hours' incubation is advisable.

In cases of extensive hæmolysis or agglutination macroscopic examination will reveal respectively a transparent reddish film or a granular opacity. This is occasionally observed at the preliminary examination, more often at the end of the first hour of incuba-

tion, but occasionally only at the final observation—hence the advisability of prolonged incubation.

For the recognition of less extensive hæmolysis or agglutination the microscope is necessary. The preparations should be examined with both low and high power dry lenses. Thus observed, specimens exhibiting no agglutination show the red cells uniformly distributed on the floor of the chamber throughout the entire area covered by the film. Careful search for cell "shadows" (the shell-like stroma of hæmolized red blood cells) is then made. The presence of any appreciable number of these should exclude the individual in question as a donor. When the hæmolysis is extensive, scarcely any cells remain intact.

Interpretation.—Any slide, both of whose chambers contain specimens which show neither agglutination nor hæmolysis, as thus described, represents blood homologous with the recipients. The donor whose identification mark such a slide bears, is a suitable one from this point of view.

TEST FOR HÆMOLYSIS AND AGGLUTINATION USED BY DR. V. P. SYDENSTRICKER, OF THE JOHNS HOPKINS HOSPITAL.

Another method of directly testing out donors against a recipient is that commonly used at the Johns Hopkins Hospital at the present time by Dr. V. P. W. Sydenstricker. It is as follows:

Blood is drawn from each donor and from the recipient, either by venopuncture or into a Wright tube from a prick in the finger or ear. At least three cubic centimeters of blood should be collected and allowed to clot to obtain clear serum. Two drops of blood are allowed to drip into 5 c.c. of 1.25 per cent. sodium citrate solution in 0.8 per cent. salt in order to obtain a suspension of corpuscles.

In performing the tests coverslips should be thoroughly clean and entirely free from dust and lint. Capillary pipettes should be used in making the preparations. We have found those drawn from 4 mm. glass tubing most satisfactory. Coverslips and pipettes should never be used more than once. One drop of donor's serum and one drop of recipient's corpuscle emulsion are placed side by side on a coverslip and thoroughly mixed by stirring with a small stirring rod made from the tip of a capillary pipette. The mixed drop should be spread out so that when the coverslip is inverted the cells will not settle to the lower part of the drop, the coverslip is then inverted over a hollow-ground slide and sealed with oil, it should be examined under the microscope at this stage to be sure that the preparation is satisfactory; the red cells should be evenly distributed over the field, touching but not overlapping one another. The process is now repeated using recipient's serum and donor's corpuscles. Con-

trols should be run on each corpuscle emulsion using salt solution instead of serum to be sure that there is no clumping of the cells in the emulsion itself.

The hanging drops should be allowed to incubate at 37° C. for one hour before hæmolysis or agglutination can be excluded. Many reactions would be avoided if this rule were strictly followed. Several instances in which agglutination and hæmolysis were absent at the end of thirty minutes have shown marked agglutination at the end of an hour. Agglutination may occur with great rapidity, however, in some cases before the specimen can be examined. Agglutination is usually easy to recognize, the cells form clumps of varying size and soon lose their identity forming a conglomerate mass in which the cell outlines can be recognized only with difficulty. Hæmolysis is often more difficult to recognize in microscopic preparations but since it is uniformly preceded by agglutination it should not be missed. When it does occur agglutination is evident but the preparation seems to have markedly fewer cells in it than when first set up, on careful focussing the "shadows" of the hæmolyzed cells can be made out and if the slide be held over a white surface the drop has a distinct yellow tinge which is not present when hæmolysis has not taken place.

When material is not available for performing the

microscopic tests the gross method may be used. The blood should be collected in the same way except that it is preferable to wash the cells used in the emulsion by centrifugalization to remove the citrate present. The centrifuged cells are then emulsified in normal salt solution, the sera and corpuscle emulsion are mixed in $\frac{1}{4}$ c.c. amounts in small test tubes and incubated for an hour. When agglutination occurs there is a "brick-dust" sediment in the tubes, the supernatant fluid being colorless; hæmolysis is present when there is the slightest red stain in the supernatant fluid.

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